

## VITAMIN D DEFICIENCY IN JAMMU IN SUBJECTS WITH NO COMORBIDITY- A PRELIMINARY STUDY

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### ABSTRACT

#### BACKGROUND

Deficiency of the vitamin D may result in metabolic bone diseases leading to rickets in children or osteomalacia in adults.<sup>1,2</sup> The vitamin D may provide protection against hypertension, cancer and multiple sclerosis.<sup>3</sup> The vitamin D level is regulated through the interaction of various factors including intestinal absorption, renal function, serum calcium level and Parathyroid Hormone (PTH).<sup>3</sup> The 2 main sources for vitamin D are synthesis in the skin on exposure to Ultraviolet-B (UVB) light from sunlight and dietary intake.

The aim of the study is to evaluate status of the vitamin D of a cohort of Jammu population with no comorbidity. A questionnaire was given to 119 patients (77 males and 42 females) where information regarding intake of calcium and vitamin D supplementation, intake of calcium rich food and exposure to vitamin D was sought.

#### MATERIALS AND METHODS

Estimation of serum 25-hydroxyvitamin D (25(OH)<sub>3</sub>) and plasma Parathyroid Hormone (PTH) intact levels was done the subjects. Serum 25 (OH) 2D3 levels did not differ significantly between males and females, although the levels were low (males 9.72 ng/mL ± 4.2 and females 8.5 ng/mL ± 4.7).

#### RESULTS

The vitamin D was still in the deficiency range even after excluding the subjects with very high PTH levels.

#### CONCLUSION

There was a high prevalence of a vitamin D deficiency in this sample of Jammu despite >70% of participants having adequate exposure to sunlight and >80% reporting adequate intake of dairy products.

#### KEYWORDS

Vitamin D, PTH, Calcium, Sunlight, Skin Preliminary Study.

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#### BACKGROUND

Deficiency of the vitamin D may result in metabolic bone diseases leading to rickets in children or osteomalacia in adults.<sup>1,2</sup> The vitamin D may provide protection against hypertension, cancer and multiple sclerosis.<sup>3</sup> The vitamin D level is regulated through the interaction of various factors including intestinal absorption, renal function, serum calcium level and Parathyroid Hormone (PTH).<sup>3</sup> The 2 main sources for vitamin D are synthesis in the skin on exposure to Ultraviolet-B (UVB) light from sunlight and dietary intake.<sup>4</sup>

Skin pigmentation may play an important role in determining vitamin D levels as darker skin colour may limit the amount of UVB light that penetrates, thereby reducing the cutaneous synthesis of vitamin D.<sup>5</sup>

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Serum 25-hydroxyvitamin D (25(OH)D) level is considered to be the best indicator of vitamin D status with reference ranges from 15 or 16 ng/mL to more than 40 or 48 ng/mL.<sup>6</sup>

A 25(OH) D level below 8 ng/mL (the threshold for development of rickets/osteomalacia) has usually been termed vitamin D insufficiency.<sup>7</sup>

We also measured the serum PTH level, which increases in response to insufficient calcium in order to stimulate bone resorption and increase the serum calcium necessary for the different biological processes in the body. An inverse relationship between PTH and 25(OH) 2D3 levels has been found in many studies.

Many studies have reported an inverse association between serum PTH concentrations and serum 25(OH)D concentrations.<sup>8-10</sup>

In areas such as Jammu where there is plentiful sunlight, it would be expected that vitamin D level would be adequate in the majority of the population. It was observed that a substantial proportion of patients as well as healthy subjects coming for routine screening have been found to have subnormal levels of vitamin D.



### Aims and Objectives

The aim of this study was to measure the vitamin D level in a cohort of healthy population in order to evaluate the vitamin D status of healthy population of Jammu.

### MATERIALS AND METHODS

**Sample-** Subjects included in this study were living in Jammu region and were apparently healthy with no associated medical problems. All subjects gave their consent to participate in the study.

A total of 119 subjects (adult males and females) were included. The study was carried out during winter between December 2008 and March 2009. Average winter temperatures in the Jammu are 14-16 degrees C during daytime.

A full clinical examination and clinical history were taken from all subjects participating in the study.

Exclusion criteria included any chronic illness, use of medication known to have effect on bone metabolism, elevated PTH level or impaired renal function.

**Data Collection-** Data was collected from subjects from that day's visit, including age, sex, height and weight and BP with questions related to medical history, sunlight exposure, exercise and general diet. Adequate exposure to sunlight was defined as regular exposure at least thrice a week between 09:30-12:30 hours for 30 minutes with at least forearms and legs exposed direct sunlight. A 15 mL blood sample was taken from each subject.

Blood was centrifuged and serum was separated and analysed promptly. Laboratory studies included measurement of random glucose, urea, creatinine, uric acid, calcium, phosphorous, alkaline phosphatase, total protein and albumin and Alanine Transaminase (ALT). These parameters were measured using a clinical chemistry analyser (dimension RxL, Siemens Diagnostics).

Serum intact PTH level was measured using an immunoassay analyser (Architect 2000i; Abbott), while serum 25(OH) 2D3 was measured using a chemiluminescence immunoassay analyser (LIAISON, DiaSorin).

### The Intra-Assay Coefficient of Variation was 11.6%-

Both high and low quality control materials were included with each run and verified to be within the expected quality control ranges before accepting the results.

The reference ranges used in our laboratory for 25 OH vitamin D were as follows- 0-5 ng/mL, (deficiency); 5-39 ng/mL, (insufficiency); and 40-100 ng/mL, (sufficiency). The reference range for other variables were- PTH 15-68.3 pg/mL, haemoglobin 12-17 g/dL, urea 7-20 mg/dL, creatinine 0.6-1.2 mg/dL, uric acid 3.4-7.0 mg/dL (males) 2.4-6.0 mg/dL (females), calcium 8.5-10.2 mg/dL, phosphorous 2.5-4.5 mg/dL, alkaline phosphatase 54-144 U/L, ALT 17-49 U/L, total protein 64-82 g/L and albumin 34-50 g/L.

Parameter	Males (n=77)	Females (n=42)
Mean (SD), age (yrs.)	33 ± 8.2	29.0 ± 7.1
Mean (SD), BMI (kg/m <sup>2</sup> )	26.5 ± 2.1	23.2 ± 2.5
Mean (SD), blood pressure (mmHg)	75.3 ± 5.6	69.1 ± 8.1
% with regular sun exposure	65	63
% with regular intake of dairy products	87	89
<b>Laboratory Parameters Mean (SD)</b>		
Haemoglobin g/dL	14.1 ± 1.2	10.9 ± 0.9
Random glucose (mg/dL)	99.4 ± 9.1	95.4 ± 10.2
Urea mg/dL	12.04 ± 7.2	11.48 ± 4.2
Creatinine mg/dL	0.94 ± 0.14	0.61 ± 0.16
Uric acid mg/dL	3.27 ± 0.9	3.05 ± 0.71
Calcium mg/dL	8.46 ± 0.02	8.58 ± 0.01
Phosphorus mg/dL	3.31 ± 0.46	3.18 ± 0.61
Alkaline phosphatase U/L	92.5 ± 29.2	72.3 ± 18.2
ALT U/L	45.3 ± 10.1	25.1 ± 6.2
Total protein g/L	74.5 ± 4.2	68.8 ± 4.9
Albumin g/L	41.5 ± 2.6	40.3 ± 3.8
PTH (pg/mL)	63.1 ± 33.2	43.7 ± 17.3
25(OH)D (ng/mL)	9.7 ± 4.2	8.5 ± 4.7

### Statistical Analysis

Normally, distributed variables were expressed as mean and Standard Deviation (SD), while variables with non-Gaussian distribution were expressed as median range and 25 to 75 percentiles. The statistical software package SPSS, version 11.0, was used for statistical testing of the data.

### RESULTS

The clinical and biochemical data of the participants are shown in Table 1.

There was no significant age difference between males and females; mean age 33 ± 8.2 years versus 29 ± 7.1 years, respectively.

A substantial percentage of male and female participants (87 and 89, respectively) reported a sufficient

regular intake of dairy products to satisfy their daily need for calcium.

Regular exposure to sunlight was reported in 63 and 65% males and females, respectively.

Males had significantly higher creatinine than in females, which is expected due to the higher body mass index of males. However, this elevated level of serum creatinine (0.94 (SD 0.14) mg/dL) was still within the laboratory reference ranges for males in this age group (0.6-1.2 mg/dL). There was no significant difference between males and females regarding fasting serum glucose, serum uric acid and total protein, albumin, phosphorous, calcium or alkaline phosphate levels. However, the mean values of serum calcium in both groups were towards the lower level of normal (8.8 mg/dL).

Males had higher ALT than females, which may be due to a mild degree of fatty liver disease in some overweight males in the sample. Serum PTH levels were significantly higher in males than females ( $P < 0.01$ ) - 63.1 (SD 33.2) versus 43.7 (SD 17.3) pg/mL, respectively. Serum 25(OH)D levels were low; mean levels in males and females were 9.7 (SD 4.2) ng/mL and 8.5 (SD 4.7) ng/mL, respectively (Figure 1). These 25 (OH)D levels did not differ significantly between males and females.

PTH levels did not correlate with serum 25(OH)D levels in either male or female groups. However, the serum 25(OH)D levels correlated with the serum calcium levels in both groups ( $r = 0.33$ ,  $P = 0.039$  and  $r = 0.3$   $P = 0.03$ , respectively).

The adjusted figures showed a serum 25(OH)D level of 9.7 (SD 4.1) ng/mL in males and 8.5 (SD 8.5) ng/mL in females, which was still within the deficiency range for serum 25(OH)D. There were no significant differences between males and females in these adjusted serum 25(OH)D levels ( $P > 0.05$ ).

Serum alkaline phosphatase levels was found to be normal in both males or females participating in the study despite the low serum 25(OH)D level reported.

## DISCUSSION

The current study evaluated serum 25(OH)D and its relationship to PTH in a cohort of healthy Jammu urban population. A high prevalence of vitamin D was found in otherwise healthy population of Jammu region.

Vitamin D plays a critical role in bone metabolism and many cellular and immunological processes.<sup>11</sup>

Low levels of vitamin D have been associated with various chronic diseases, especially osteoporosis.<sup>12,13</sup>

Vitamin D is synthesised in the skin through exposure to UVB radiation and solar radiation is the primary source of vitamin D for most people.<sup>14</sup>

Vitamin D is also acquired from the diet from sources where it occurs naturally (such as fatty fish, fish oil and eggs), from fortified products (such as milk and orange juice) and from supplements.<sup>15</sup>

In areas far from the equator, the amount of UVB available from sunlight during the winter months is inadequate to allow cutaneous vitamin D synthesis.

However, in Jammu, there should be sufficient sunlight to allow for vitamin D synthesis.<sup>16</sup>

Different factors can affect serum vitamin D level including skin pigmentation (synthesis decreases in dark skin), ageing (vitamin D synthetic capacity decreases with ageing), the use of sun-blocking agents, chronic renal, liver and gastrointestinal tract diseases and the use of certain medications (e.g., anticonvulsants).<sup>17</sup>

Low levels of serum vitamin D and calcium exert a positive feedback on serum PTH to increase serum calcium level that stimulates the conversion of 25(OH)D to vitamin D and to increase the absorption of vitamin D from the gut.

Different studies that have elevated the status of vitamin D in different ethnic populations suggest concentrations  $< 10$ -11 ng/mL as deficiency.<sup>18,19</sup>

Lower levels are expected to be associated with calcium malabsorption and hypocalcaemia, severe hyperparathyroidism and vitamin D rickets or osteomalacia.<sup>20</sup>

The current study found a marked deficiency in the serum 25(OH)D level in both male and female patients.

The low level of 25(OH)D found in the current study could not be explained by low intake or poor sun exposure as a substantial proportion of the participants in this study (87% of males and 89% of females) reported a sufficient nutritional intake of vitamin D and nearly 67% of them had regular exposure to UV sunlight.

A possible explanation of this markedly low 25(OH)D level in both males and females is a racial difference in vitamin D concentration or a genetic predisposition to vitamin D deficiency among Jammu population.

Pal et al reported an extremely high prevalence of 25(OH)D deficiency among Asians.<sup>20</sup>

Another possible explanation of these low 25(OH)D levels in our cohort of patients is that women in hilly areas in Jammu wear the traditional veil, which prevents the penetration of the UVB light needed for the synthesis of vitamin D.

Certainly, Hobbs et al reported severe vitamin D deficiency in Arab-American women who wear the veil.<sup>21</sup>

However, this does not explain why Jammu men had similarly low levels of vitamin D.

Even if we hypothesise that Jammu have a mildly dark skin, which could limit the penetration of UVB light, over 90% of participants reported an adequate intake of calcium and vitamin D rich food products is which should compensate for a lack of cutaneous synthesis of vitamin D.

## CONCLUSION

This suggests that there are racial differences in the absorption of calcium and vitamin D from the gut. An important finding is that we could not find a correlation between serum 25(OH)D and PTH levels and the mean serum 25(OH)D level was still in the lower end of the reference range even after exclusion of patients with high PTH levels.

In other words, although vitamin D levels were markedly reduced, the PTH level was not increased in the majority of participants.

This finding agrees with Haarbarger et al who found that the subnormal 25(OH)D level in their study was also not related to hypocalcaemia or a significant rise in PTH. They suggested that 25(OH)D measurements should be requested when vitamin D deficiency is clinically suspected irrespective of calcium and PTH biochemical results.<sup>22</sup>

This study has presented a preliminary evaluation of vitamin D status in young apparently healthy Jammu population. This study showed that the prevalence of 25(OH)D deficiency was high among Jammu and suggest the need to increase the fortification of food products with vitamin D and screening for vitamin D deficiency, but also young Jammu adults to prevent future morbidity. Future studies should include evaluation of bone mineral density and comparison with the reference range for adults of similar age and sex.

Other studies are needed to measure the degree of skin pigmentation quantitatively and its correlation to vitamin D level and to monitor biochemical parameters after vitamin D supplementation.

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