

# Changing Trend in Vitamin D Status from 2008 to 2016: An Experience from a Tertiary Care Institute in North India

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## Abstract

**Background:** Serum 25-hydroxyvitamin D (25(OH)D) assays have become readily available in India over the past decade. A large number of cross-sectional studies have been performed on the vitamin D status and the prevalence of vitamin D deficiency (VDD) in India. However, seasonal and long-term trends in serum 25(OH)D levels have been reported less frequently. **Aim:** To determine the seasonal and year-wise variation in vitamin D status at a tertiary care hospital in north India. **Materials and Methods:** Using hospital records, the data on serum 25(OH)D assays performed in its endocrinology laboratory between 2008 and 2016 were obtained. For analysis of seasonal trends, the months of a year were divided into following seasons: March to June (summer season), July to October (rainy season), and November to February (winter season). VDD was defined as serum 25(OH)D concentration <20 ng/mL. **Results:** A total of 26,339 assays of serum 25(OH)D were analyzed in the study. The year-wise assay numbers increased steadily from 2008 to peak in the year 2012, followed by a decline and a second smaller peak in the year 2016. The mean serum 25(OH)D concentration increased from 19.1 ± 16.4 ng/mL in 2008 to 21.7 ± 17.1 ng/mL in 2016 ( $P = 0.02$ ). Between 2008 and 2016, the prevalence of VDD decreased from 71.9% to 54.3% in females, and from 56.7% to 52.1% in males. The levels in rainy season were significantly higher as compared to winters and summers ( $P < 0.05$  for both). Hypervitaminosis D (serum 25(OH)D >100 ng/mL) and vitamin D toxicity (serum 25(OH)D >150 ng/mL) were seen in 319 (1.2%) and 27 (0.1%) assays, respectively. **Conclusions:** This study provides data on seasonal and year-wise trends in vitamin D status over a long period of time at a tertiary care hospital in north India. A long-term trend toward improving vitamin D status, especially in females, was noted in the study. The prevalence of VDD was found to decrease in the analyzed samples during the study period.

**Keywords:** 25-hydroxyvitamin D, seasonal, trend, vitamin D deficiency, vitamin D toxicity

## INTRODUCTION

Vitamin D deficiency (VDD) has been described as the most common nutritional deficiency, and possibly the most common medical condition globally.<sup>[1]</sup> In humans, vitamin D can be obtained through cutaneous synthesis (following sunlight exposure), some natural foodstuffs (such as oily fishes), fortified foodstuffs (such as fortified milk), and exogenous supplements (such as cholecalciferol and ergocalciferol).<sup>[2]</sup> 25-hydroxyvitamin D (25(OH)D) is the most abundant circulating metabolite of vitamin D and is considered to be the most robust and reliable marker of vitamin D status.<sup>[3,4]</sup> Serum 25(OH)D assays have become readily available in India over the past decade. A large number of cross-sectional studies have been performed on serum 25(OH)D levels and the prevalence of VDD in India.

Despite adequate sunshine, VDD has been widely reported across various age groups and regions of our country.<sup>[5-15]</sup> Several factors contribute to this observation—sun fleeing behavior due to the fear of darkening, increased skin pigment, clothing habits, increased atmospheric pollution (especially in Northern India), and lack of adequate dietary sources of vitamin D available. Owing to the ease of assay availability

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and improved understanding of this condition among health care providers, the use of vitamin D supplements has become more liberal. Therefore, it becomes important to study the evolution of the landscape of VDD in this peri-supplementation era. An improving trend in vitamin D status has been reported in studies from the USA (2007–2017), Ireland (1993–2013), Norway (1994–2008), and Canada (over 10 years of follow-up).<sup>[16–19]</sup> A seasonal variation in vitamin D status and a concerning trend of hypervitaminosis D was also reported in these studies. Although vitamin D toxicity has been increasingly reported in the last decade,<sup>[20–25]</sup> unfortunately, the data on seasonal and year-wise trends in vitamin D status from India are scarce.<sup>[25,26]</sup>

With this background, this study aims at reporting the data on seasonal and year-wise variation in vitamin D status based on serum 25(OH)D measurements performed between 2008 and 2016 at a tertiary care hospital in north India.

## MATERIALS AND METHODS

### Data collection

We obtained the data on serum 25(OH)D assays performed in the endocrinology laboratory of a tertiary care hospital in north India (All India Institute of Medical Sciences, New Delhi) from January 2008 to February 2017. Since the data for the year 2017 were only available for the first two months, the analysis was mainly based upon samples derived from the years 2008 to 2016. The demographic details (age and gender), date of the performance of the assay, and patient status (inpatient or outpatient) were also noted. Because the data were derived from lab records, details of the medical condition and the history of use of vitamin D supplements were not available. For analysis of seasonal trends, the months of a year were divided into following seasons: March to June (summer season), July to October (rainy season), and November to February (winter season). Since serum 25(OH)D and parathyroid hormone (PTH) measurements are often requested simultaneously by a clinician, data for serum intact PTH (iPTH) were also retrieved (wherever available) to evaluate the relationship between the two. Observations with serum iPTH >2000 pg/mL were excluded from the analysis as these were considered to result either from severe secondary or primary hyperparathyroidism.

### Definitions used in the study

Serum 25(OH)D concentration <20 ng/mL and serum iPTH concentration >65 pg/mL were defined as VDD and secondary hyperparathyroidism, respectively. Serum 25(OH)D concentration >100 ng/mL and >150 ng/mL were defined as hypervitaminosis D and vitamin D toxicity, respectively.

### Hormone assays

Serum 25(OH)D was estimated by chemiluminescent tracer-based competitive immunoassay (LIAISON, DiaSorin Inc., Stillwater, MN, USA). Serum iPTH was estimated using electrochemiluminescent tracer-based immunometric

assay (Elecsys-2010, Roche Diagnostics, Mannheim Germany; lower detection limit: 1.2 pg/mL, normal range: 15–65 pg/mL). 25(OH)D assays were performed manually till 2010 and with the help of an autoanalyzer subsequently, however, Diasorin kits were used for both the methods.

### Statistical analysis

Statistical analysis was carried out using Stata 11.0 (College station Road, TX, USA). Data were presented as number (%) and mean ( $\pm$ SD), as appropriate. Qualitative variables were compared using the Pearson Chi-square test, while the student's *t*-test was used for normally distributed quantitative variables. For analysis of trends in serum 25(OH)D levels, regression analysis was performed. A *P* value of <0.05 was considered statistically significant.

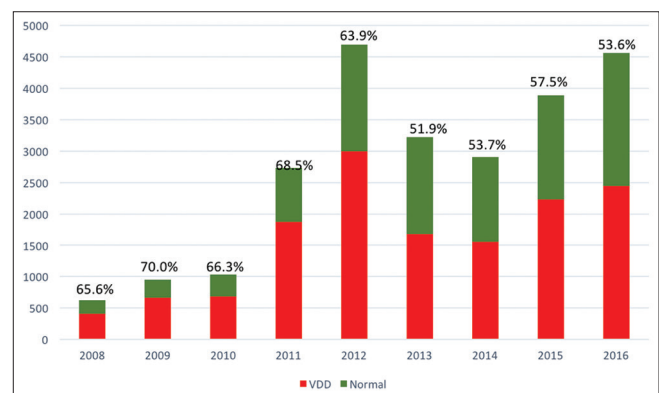
## RESULTS

### Baseline characteristics

A total of 26,339 assays of serum 25(OH)D performed between January 2008 and February 2017 were analyzed in the study [Figure 1]. Of these, 843 (3.2%) assays were ordered from the inpatient department, while the rest 25,496 (96.8%) were ordered from outpatient departments (endocrine as well as non-endocrine). The year-wise assay numbers increased steadily from 2008 to peak in the year 2012, followed by a decline and a second smaller peak in the year 2016 [Figure 1]. The mean age of patients who submitted their samples was  $37.3 \pm 18.3$  years. Of the total 26,070 assays for which sex details were known, 9,350 (35%) and 16,720 (65%) were performed in males and females, respectively.

### Change in serum 25(OH)D concentration over the years

The mean serum 25(OH)D concentration increased from  $19.1 \pm 16.4$  ng/mL in 2008 to  $21.7 \pm 17.1$  ng/mL in 2016 (*P* = 0.02). The mean serum 25(OH)D concentration remained below 20 ng/mL between 2008 and 2011, followed by a steep rise to a peak of 23.7 ng/mL in 2013. Subsequently, the levels gradually decreased to 21.7 ng/mL in 2016. The year-wise distribution of mean serum 25(OH)D concentration has been depicted in Figure 2.



**Figure 1:** Year-wise number of observations with normal vitamin D levels and vitamin D deficiency (VDD). The prevalence of VDD in a given year has been shown as a percentage

### Prevalence of VDD over years

Overall, evidence of VDD was seen in 15,593 (59.2%) samples analyzed. Of all samples with VDD, 5,629 (36.1%) had evidence of secondary hyperparathyroidism. The prevalence of VDD was almost equal in males (58.6%) and females (59.6%). The year-wise prevalence of VDD for the study population has been presented in Figure 1. The prevalence of VDD for the entire study population decreased from 65.6% in 2008 to 53.6% in 2016. This fall was steeper in females (71.9% in 2008 to 54.3% in 2016), compared to males (56.7% in 2008 to 52.1% in 2016).

### Seasonal variations of serum 25(OH)D levels

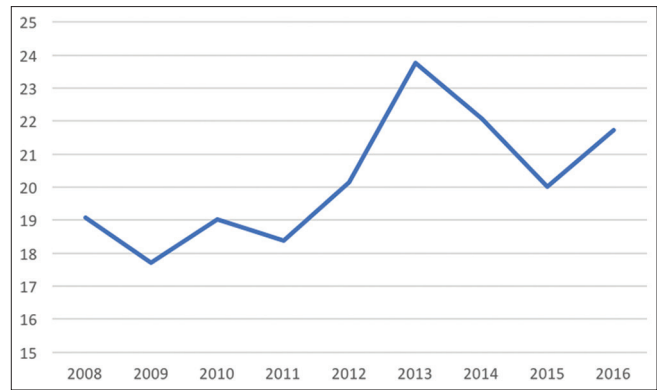
Serum 25(OH)D levels in the rainy season were significantly higher as compared to winters ( $23.0 \pm 22.4$  vs  $20.6 \pm 23.3$  ng/mL,  $P < 0.05$ ) and summers ( $23.0 \pm 22.4$  vs  $20.8 \pm 23.5$  ng/mL,  $P < 0.05$ ) [Figure 3]. The overall odds ratios for serum 25(OH)D concentration below 10 ng/mL in the rainy season (compared to the winter season) was 0.58 (95% CI 0.54, 0.63,  $P < 0.05$ ) and 0.52 (95% CI 0.44, 0.62,  $P < 0.05$ ) for those aged above and below 18 years, respectively.

### High serum 25(OH)D levels

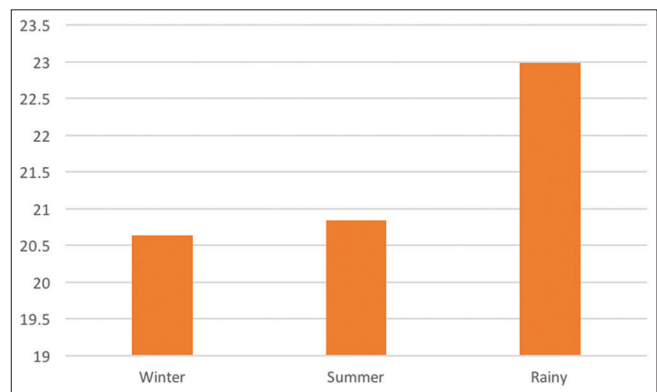
Serum 25(OH)D concentration  $>100$  ng/mL (hypervitaminosis D) was seen in 319 (1.2%) assays (43% females and 57% males). Serum 25(OH)D concentration  $>150$  ng/mL (vitamin D toxicity) was seen in 27 (0.1%) assays (16 females and 11 males). The mean age of patients with hypervitaminosis D and vitamin D toxicity was  $36.0 \pm 23.6$  years (range: 1–97 years) and  $31.5 \pm 21.1$  years (range: 2–84 years), respectively. Vitamin D toxicity was observed in 17 assays between 2008 and 2012 and 10 assays between 2013 and 2016 [Figure 4]. Sixty-seven percent of all cases of vitamin D toxicity were derived from the period between 2011 and 2013 (which also showed a sharp rise in mean serum 25(OH)D levels).

## DISCUSSION

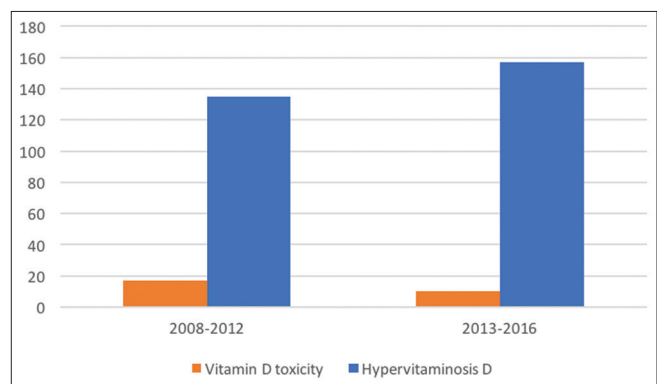
With the increased availability of serum 25(OH)D assays, VDD has been increasingly recognized as a public health problem.<sup>[1,2]</sup> At the same time, awareness about this condition and its prevention and treatment have also increased among health care providers. Serum 25(OH)D levels have been shown to increase over long periods in several Western countries.<sup>[16–19]</sup> In-line with these observations, our study also shows an increase in serum 25(OH)D levels, as well as a decrease in the prevalence of VDD from 2008 to 2016. Since food fortification with vitamin D is still in its initial stages in our country, this improvement is likely to be caused by increased pharmacological supplementation. Data from the pharmaceutical industry suggest that the vitamin D market size in India rose from 2.98 billion (INR) in 2014 to 5.38 billion (INR) in 2018.<sup>[27]</sup> This increase in market size is likely to be reflected in increased supplementation and rising mean serum 25(OH)D levels. Interestingly, the increase in serum 25(OH)D levels and the decline in the prevalence of VDD was more in females compared to males. This can be



**Figure 2:** Change in the mean serum 25(OH)D concentration over the years. The mean serum 25(OH) concentration (ng/mL) and the corresponding year have been depicted on the Y and X axes, respectively



**Figure 3:** Mean serum 25(OH)D concentration in each season across the study period. The mean serum 25(OH) concentration (ng/mL) and the corresponding season have been depicted on the Y and X axes, respectively



**Figure 4:** Observations with hypervitaminosis D and vitamin D toxicity across the two study periods (2008–2012 and 2013–2016)

attributed to a greater awareness of the perils of VDD (in females) among physicians in India, leading to a greater increase in vitamin D supplementation in this group. VDD has been reported to be higher in females as compared to males in both urban and rural populations in India.<sup>[5–7,14]</sup>

The prevalence of VDD in healthy individuals in India has been reported to vary from 51% to 91% in different population-based

studies conducted in diverse population groups.<sup>[5-13]</sup> Most of these cross-sectional studies were performed in the community with small sample sizes except the one by Marwah *et al.* which included 5,137 adolescents (10–18 years) and found a mean serum 25(OH)D level of  $11.8 \pm 7.2$  ng/mL.<sup>[12]</sup> Shukla *et al.* reported serum 25(OH)D levels in 26,346 ostensibly healthy individuals visiting a private hospital for a routine health checkup between 2011 and 2014.<sup>[26]</sup> They found VDD in 59% (61% males and 31% females) of the study participants. Similarly, Sharma *et al.* reported data of 5,527 patients from a tertiary care hospital in north India.<sup>[25]</sup> They found VDD in 59.4% of the patients with a decreasing trend from 2011 to 2016. The prevalence in our study appears to be in-line with these studies, reflecting the poor vitamin D status of patients visiting this hospital. However, this appears to be related to an overall VDD in the population, with a probable worsening in otherwise ill patients.

The data on seasonal variation in serum 25(OH)D levels are scanty. The study by Sahu *et al.* reported that mean serum vitamin D levels were almost twice as high in summer as compared to winter months in a rural population in north India.<sup>[13]</sup> Similarly, in the hospital-based study by Shukla *et al.*, serum 25(OH)D level was significantly lower during winter-spring seasons compared to the summer-autumn season.<sup>[26]</sup> The seasonal changes in serum 25(OH)D appear to reflect increased exposure to sunlight and increased vitamin D synthesis during summer months. This is reflected in the form of higher serum 25(OH)D levels in the following season, namely the rainy season in our study. The lowest vitamin D levels were seen in winters which are expected considering the increased solar zenith angle, decreased sunlight exposure due to the cloth covering, and increased atmospheric pollution (due to stubble burning in this season in northern India) during this period. We, however, acknowledge that the contribution of atmospheric pollution to this observation may be quite variable as patients treated at this hospital come from different parts of the country.

Our study found hypervitaminosis D in 319 (1.2%) and vitamin D toxicity in 27 (0.1%) measurements, while Sharma *et al.* (n-5527) reported hypervitaminosis in 225 (4.7%) and vitamin D toxicity in 151 (2.8%) patients.<sup>[25]</sup> We found that the prevalence of hypervitaminosis D peaked in the year 2013, followed by a steep decline in the next 2 years (2014 and 2015), and a gradual increase over the remaining period. These findings mirror the trend in mean serum 25(OH)D levels in our study. Hypervitaminosis D is an increasingly recognized problem mostly due to overzealous supplementation or prescription errors. The likelihood of this condition has increased in the current scenario as a result of increased awareness of VDD among the treating physicians. It is probable that such an increase in awareness (between 2011 and 2013) contributed to an increase in mean serum 25(OH)D concentration as well as the prevalence of hypervitaminosis D. Vitamin D toxicity was reported as early as 2 years in our study. The occurrence of this condition in the pediatric age group is a major cause of concern since nephrocalcinosis and renal dysfunction resulting

from an early insult may have long-lasting implications.<sup>[28,29]</sup> There is an urgent need to create awareness about this “other side of vitamin D problem” among healthcare providers.

The strengths of our study are that it reports the longitudinal and seasonal trends in serum 25(OH)D levels from an endocrine laboratory at a tertiary care center over a long period of time. The evolving threat of hypervitaminosis D has also been brought about in this study. Our study has several limitations. The study samples were derived from patients visiting a tertiary care hospital, and hence, the results cannot be generalized to a healthy population in the community. However, considering a large number of samples and our hospital policy of not repeating serum 25(OH)D levels after treatment of VDD (unless suspecting hypervitaminosis D or vitamin D toxicity), the data may provide some insights about the vitamin D status of the community. Additionally, since the hospital records of the endocrine laboratory were used to derive the data, we could not analyze the effects of undocumented preexisting supplementation and confounding medical conditions on serum 25(OH)D levels.

To conclude, our study reports seasonal and year-wise trends in serum 25(OH)D levels over a long period of time at a tertiary care hospital in north India. We noted a long-term trend toward increasing serum 25(OH)D levels and a decrease in the prevalence of VDD in both genders, especially females. It is likely that increased awareness about VDD and its prevention and treatment among physicians accounted for this observation.

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### Conflicts of interest

There are no conflicts of interest.

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