

## A Study of “Osteoporosis due to lack of Vitamin - D deficiency” through a small Survey in Kolkata, (West Bengal)

S Rehan Ahmad\*

Assistant Professor, H M M College for Women, Kolkata, W.B, India

\*Corresponding Author E-mail: [zoologist.rehan@gmail.com](mailto:zoologist.rehan@gmail.com)

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### ABSTRACT

*Bone loss and osteoporosis with the resultant increase in fracture risk should be major concerns for patients and health care providers. As the population ages, the long-term effects of osteoporosis including pain, loss of independence and institutionalized care will become more prevalent. Efforts to prevent bone loss and osteoporosis should start with proper education about a healthy lifestyle, including optimal calcium and vitamin D and exercise in adolescence. This education should continue throughout life, with emphasis during times of increased bone loss such as the menopause transition. This paper reviews the cornerstone of bone health; calcium and vitamin D. Although dietary sources of both nutrients are available, most people do not receive adequate amounts for proper bone health. In addition, the heightened awareness of damaging effects of sunlight has limited vitamin D synthesis from the skin. Fortunately, supplements are available that can supply the body with amounts necessary for bone health.*

**Keywords:** Osteoporosis, Vitamin – D, Kolkata, West Bengal.

### INTRODUCTION

A human body produces vitamin D as a response to sun exposure. A person can also boost their vitamin D intake through certain foods or supplements. Vitamin D is essential for several reasons, including maintaining healthy bones and teeth. It may also protect against a range of diseases and conditions, such as type 1 diabetes. Despite its name, vitamin D is not a vitamin, but a prohormone, or precursor of a hormone. Vitamins are nutrients that the body cannot create, and so a person must consume them in the diet.

However, the body can produce vitamin D. In this article, we look at the benefits of vitamin D, what happens to the body when people do not get enough, and how to boost vitamin D intake.

Vitamin D plays a pivotal role in calcium and mineral metabolism. It is astonishing to find vitamin D deficiency in India despite plentiful sunlight. This could probably be because of urbanization, life style and dress code changes, and revision of vitamin D adequacy range.

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Recent studies in south India using in vitro ampoule model with 7-dehydrocholesterol have shown adequate formation of active form of vitamin D in mid-day sun. In India 70% of populations reside in rural areas. Only 35% of Indian populations have access to regulated milk supply. We as humans can get vitamin D from abundant sunshine, by exposing 18% of body surface area (without sunscreen) to mid-day sun for 30-45 min to cause 1 minimal erythemal dose (MED) which is equivalent to taking about 600 to 1000 IU of vitamin D. This is about the recommended daily dose by expert group on human nutrient requirements and the dose used in studies with fortified milk supplementation studies. Vitamin D synthesized in the skin lasts two-times longer in the body. In populations where there is limited exposure to sunlight, like dress-code limiting sun-exposure, usage of sunscreen with (SPF) greater than 8 etc., vitamin D supplementation may also be required. Since there is widespread calcium deficiency in Indian population, calcium supplementation should be an integral part of vitamin D supplementation therapy. For most people, the main source of vitamin D is skin exposure to sunlight. Exposure to ultraviolet-B (UV-B) photons (290–315 nm), causes the photolysis of 7-dehydro-cholesterol to pre-vitamin D<sub>3</sub>, which thermally (37 °C) isomerizes to vitamin D<sub>3</sub> by a membrane enhanced mechanism. It has been a general belief that vitamin D deficiency is an uncommon problem in India because of abundant sunshine. 6 There is, however, now increasing evidence that this is not true and it has been observed that Vitamin D deficiency is widespread across the country and in all age groups. 7 This could probably because of urbanization, life style and dress code changes in the country or the revision of normative ranges of vitamin D sufficiency. Many factors influence the production of vitamin D<sub>3</sub> in the skin. In general, the cutaneous production of vitamin D declines with age. 8 An alteration in the zenith angle (angular distance between sun and object directly underneath) of the sun caused by a change in latitude, season of the year, or time

of day dramatically influences the skin's production of vitamin D<sub>3</sub>. 9 In a study<sup>7</sup> designed to demonstrate and calculate the efficacy of sunlight on synthesis of vitamin D at different zenith angles, calculations, using linear regression modelling, have revealed that reduction in every one degree of angle leads to increase in vitamin D by 0.285 units. 7 Attenuating factors such as clothing, duration of exposure to sunlight (intense heat in tropics preventing people from sun exposure), type of skin (proportionately high melanin in equatorial regions), pollution (e.g., Asian brown cloud phenomenon), 7 and increasing indoor life-style have all been blamed for this now recognized widespread problem. Even in hot and arid countries of the Middle East, vitamin D status has been demonstrated to be very low in summer [97% have 25OHD levels less than 30 ng/mL and 85.2%] had vitamin D deficiency.

#### **Sunshine vitamin**

The Food and Agricultural Organization (FAO)/ World Health Organization (WHO) Expert Consultation states that the most physiologically relevant and efficient way of acquiring vitamin D, in most locations in the world around the equator (between latitudes 42° N and 42° S) is to synthesize it endogenously from skin from 7-dehydro-cholesterol present in the subcutaneous fat by minimum of 30 minutes of skin exposure (without sunscreen) of the arms and face to mid-day sun.<sup>11</sup> It has been concluded from the experimental data that exposure of the body in a bathing suit (almost 100% of body surface area) to sunlight that causes slight pinkness of the skin is equivalent to ingesting approximately 20,000 IU of vitamin D orally. Therefore, exposure of 6% of the body to 1 MED is equivalent to taking about 600 and 1,000 IU of vitamin D. Applying the rule of nines used in burns, exposure of both forearms, and face is 12% of body surface area. For Caucasian skin (type 2 or 3), exposing face, arms and legs for a period equal to 25% of the time that it would take to cause 1 MED, for two-to three-times a week can satisfy the body's vitamin D requirement while

minimizing sun damage. Compared to Caucasians, Asians have darker skin (type 4 or 5) and, therefore, with the same amount of MED, they would require greater duration of exposure than their light skinned counterparts to synthesis comparable amount of vitamin D<sub>3</sub>.

### Review of Literature:

Vitamin D deficiency is pandemic, yet it is the most under-diagnosed and under-treated nu deficiency in the world. Vitamin D deficiency is widespread in individuals irrespective age, gender, race and geography. Vitamin D is photosynthesized in the skin on exposure to UV Sun exposure alone ought to suffice for vitamin D sufficiency. However, vitamin D deficit widely prevalent despite plentiful sunshine even in tropical countries like India. Vitamin D deficiency has a bearing not only on skeletal but also on extra skeletal diseases to its multifarious implications on health, the epidemic of vitamin D deficiency in India to significantly contribute to the enormous burden on the healthcare system of India. Cult social taboos often dictate lifestyle patterns such as clothing—that may limit sun expos vegetarianism—which certainly limits vitamin D rich dietary options. Most Indians are vegetable the socioeconomically backward people constitute a large percentage of the population in underprivileged generally suffer from overall poor nutrition. Vitamin D rich dietary sources are and unaffordable to most Indians. Vitamin D supplements are available, but most Indians aware that they need additional vitamin D. Additionally, the cost of these supplements is es prohibitive to the majority. Fortification of staple foods with vitamin D may prove to be a mor solution towards attaining vitamin D sufficiency in India. There are scores of research papers in the literature reporting poor vitamin D status from India and some from other countries of the Indian subcontinent too. These research papers ha included in this review. Many of these studies measured serum 25-hydroxyvitamin D 1 ostensibly healthy subjects. Biochemical evidences of suboptimal bone health are elevated phosphatase (ALP)

and elevated PTH levels (secondary hyperparathyroidism or SHPT). The often reported in research papers, especially with respect to their correlation with vitamin D However, the most accurate and convincing measure of bone mineral density (BMD) is DEX Energy X-ray Absorptiometry). Research articles reporting BMD, as measured by DEXA context of vitamin D status of ostensibly healthy individuals, are few. BMD data, as they co with the vitamin D status in ostensibly healthy Indians is compiled. A few articles also reported of interventions studies such as vitamin D supplementation and vitamin D fortified foods. The aim of the paper is to impress upon the practicing physicians in India about the gravy vitamin D deficiency problem throughout India, so that they may take necessary caution and the diagnosis and treatment of vitamin D deficiency. Additionally, this article may also serve the case to the Health ministry, and the Food and Nutrition Board in India for population strategy of fortification of staple foods with vitamin D. This paper provides a comprehensive p the vitamin D status of ostensibly healthy Indians, countrywide. The most reliable marker of vi status is the serum concentration of 25(OH) D. In the publications, investigators reported their 25(OH) D levels either as nm. (nanomoles per litter) or ng/mL. To simplify information and for of comparison, in this review all the data on 25(OH) D levels are presented in a single concern unit for serum 25(OH) D levels—ng/mL. Most investigators have used different cut-off levels t vitamin D deficiency, insufficiency and sufficiency levels. While some may have done so preference perhaps, other investigators defined their own cut-off levels as determined by the regression between 25(OH) D levels and PTH levels. Therefore, to further facilitate comparison.

### Vitamin D Metabolism

Vitamin D can be synthesized in sufficient amounts by most vertebrates on adequate exp the skin to sunlight (UVB rays). It is critical that most vertebrates obtain a sufficient amount of D either from their diet or from

adequate exposure of the skin to sunlight. The term “vitamin D” encompasses vitamin D<sub>3</sub> (cholecalciferol) or vitamin D<sub>2</sub> (ergocalciferol). Vitamin D<sub>3</sub> is produced in the skin on exposure to sunlight. Vitamin D<sub>3</sub> is derived from 7-dehydrocholesterol by ultraviolet irradiation of the skin. Vitamin D<sub>3</sub> is also found in animal food sources e.g., fatty fish (e.g., mackerel and tuna) cod liver oil, milk, etc. Vitamin D<sub>2</sub> is found in vegetal sources like sun-yeast and mushrooms. Notably, most dietary sources are not sufficiently rich in their vitamin D content. Vitamin D (both forms D<sub>3</sub> or D<sub>2</sub>) is a prohormone which requires two hydroxylations to attain its biologically active form—1,25 (OH)<sub>2</sub>D. The first hydroxylation occurs in the liver, at C<sub>25</sub> to form 25-hydroxyvitamin D, also known as 25(OH)D or calcidiol. 25(OH)D is the circulating form of vitamin D. The second hydroxylation occurs at position C<sub>1α</sub> to form 1,25 (OH)<sub>2</sub>D, also known as calcitriol. 1,25 (OH)<sub>2</sub>D is produced primarily in the liver but not exclusively in the liver. 1,25 (OH)<sub>2</sub>D is released in blood, where it binds to vitamin D binding protein (DBP) and reaches target tissues to exert its endocrine functions through the vitamin D receptor (VDR). 1,25 (OH)<sub>2</sub>D is also produced in several extrarenal tissues for its paracrine and autocrine functions. Most cells have VDR. Many cell types can also produce 1,25 (OH)<sub>2</sub>D. 1,25 (OH)<sub>2</sub>D is capable of regulating a wide variety of genes that have important functions in regulating cell growth and differentiation.

### **Vitamin D and Skeletal Health**

Rickets, osteomalacia and osteoporosis are widely prevalent all over the world. The most recognized function of 1,25 (OH)<sub>2</sub>D involves regulation of calcium and phosphorus balance, mineralization and remodelling. Without adequate levels of 1,25 (OH)<sub>2</sub>D in the bloodstream, calcium cannot be absorbed. Low calcium levels lead to an increase in serum PTH-related protein which leads to increased tubular reclamation of calcium in kidneys and resorption from the cost of lowering bone density. In the long term this leads to weakened and brittle bones that easily fracture. Approximately 40%–60% of total skeletal mass at maturity is accumulated.

Vitamin D deficiency and insufficiency are the major causes of vitamin D deficiency. Poor nutrition, deprivation of sunlight, consequent decline in the synthesis of cutaneous vitamin D<sub>3</sub> and decreased renal hydroxylation of 25 (OH)D by the ageing kidney. Long-lasting and severe vitamin D deficiency leads in adults to osteomalacia and in children to rickets (a bone disorder characterized by typical biochemical and bone abnormalities), along with defective mineralization, severe secondary hyperparathyroidism, hypocalcaemic, hypophosphatemia and an increase in total alkaline phosphatase. Vitamin D deficiency can be confirmed by measuring 25 (OH)D levels which are usually very low and often undetectable. The prevalence is high in the institutionalized and housebound elderly population. Vitamin D insufficiency (subclinical vitamin D deficiency) is increasingly being recognized as a distinct pathological entity. In contrast to vitamin D deficiency, it is characterized by mild secondary hyperparathyroidism, normokalaemia and normal bone mineralization. The initial fall in ionized plasma calcium stimulates parathyroid hormone secretion, which in turn stimulates renal 1α-hydroxylase and increases 1,25 (OH)<sub>2</sub>D production. This restores serum calcium to the normal set-point for that individual, but at the expense of increased bone turnover, and prevents the emergence of osteomalacia.

### **Vitamin D therapy**

Lips et al. and Ooms et al. (2001) have shown that daily supplementation with small doses of vitamin D<sub>2</sub> or vitamin D<sub>3</sub> (10–20 mg/day) can reduce the secondary hyperparathyroidism induced by vitamin D insufficiency and increase bone mineral density, but there have been no prospective randomized controlled trials to evaluate the effect on vertebral fracture rates. Studies on hip fracture reduction, as with calcium, have produced conflicting results. Lips et al. showed that 400 IU vitamin D daily for three and a half years had no effect on reducing hip fractures and, although most subjects were vitamin D-replete, further sub-analysis on the vitamin D-

deficient patients similarly showed no significant reduction in hip fracture rate. In contrast, Heikinheimo et al. showed that vitamin D given annually by intramuscular injection (300 000 IU) resulted in a decrease in non-vertebral fractures, although sub-analysis only showed a statistically significant reduction in upper limb but not hip fractures. No studies have evaluated the effect of vitamin D in the reduction of second hip fracture in patients with vitamin D insufficiency.

#### **Combination vitamin D and calcium**

The use of combination vitamin D and calcium therapy has nevertheless shown a consistent reduction in non-vertebral fractures. showed that supplementation with 1.2 g calcium and 800 IU vitamin D<sub>3</sub> over 18 months resulted in a 43% reduction in hip fractures and a 32% reduction in the total number of non-vertebral fractures in institutionalized, vitamin D-insufficient elderly women compared with the placebo group, with a mean reduction of 47% in secondary hyperparathyroidism. Previous osteoporotic fractures were present in some of these patients, but sub-analysis of prevalent fractures and the reduction in second fractures was not carried out. Dawson-Hughes and co-workers' study of patients over the age of 65 years living at home showed that treatment for 3 years with 500 mg of calcium plus 700 IU of vitamin D<sub>3</sub> increased bone mineral density at both hip and spine. The reduction of non-vertebral fractures was of a similar magnitude to that in Chapuy and co-workers' study, but the absolute numbers of fractures in the study were small. In this study it was unclear what proportion of patients were vitamin D-insufficient, although there was a 33% mean reduction in parathyroid hormone.

### **MATERIALS AND METHODS**

#### **Research design**

Research design organised by three phases, are as follows:

**1<sup>st</sup> phase:** Selected a small sample from old age home. And taking permission from old age home authority for organise a health camp.

**2<sup>nd</sup> phase:** Requesting every participant to enrols their name for this camp and discuss

about study of Osteoporosis due to lack of vitamin D deficiency.

**3<sup>rd</sup> phase:** At last, organise a survey by an interview and questionnaire method. After completing data analysis, a free vitamin D awareness camp held by the Health centre.

These data clearly raise two important concerns. Firstly, at the population scale in short term at least, simple supplemental doses without adequate loading doses may not be sufficient to achieve therapeutic levels particularly in those who would benefit from immediate increase (e.g., elderly at risk of osteoporotic fractures) and secondly, fortification/supplementation of vitamin D if not sustained in long term may not yield desired vitamin D levels and health benefits. Hence despite fortification there will be a need for appropriately treating 'at risk' groups with therapeutic doses in a supervised environment and an equal need for vigilance of the fortification programme with robust and continued quality assessment to ensure its long-term success. There are no Indian guidelines for evaluation, treatment and prevention of vitamin D deficiency.

#### **Population of the study**

I am going to an old age home and collect 50s data of Osteoporosis patients and their x-ray report.

Many of them suffering from vitamin D deficiency.

#### **Tools and technique used for data collection**

A health centres were invited to attend a workshop designed for explaining the study objectives and procedure in Osteoporosis patients of old age home. At enrollment, for each participant a questionnaire that included information on sociodemographic, anthropomorphic, behavioral, and Vitamin d characteristics was completed by a trained interviewer. Weight was measured with minimum clothing to the nearest 100 grams. Height was measured with a tape measure in standing position with normal posture of shoulders. Body mass index was calculated by dividing weight (kg) on height (m<sup>2</sup>). Systolic and diastolic blood pressures (SBP and DBP) were measured twice in a sitting position with

a standard mercury sphygmomanometer after a 15-min rest and the mean of the 2 measurements was considered as SBP or DBP. All previous x-ray report collected from patient and new x- ray done for diagnosis.

### **Procedure of data collection**

#### **Types of Research Data**

Data may be grouped into four main types based on methods for collection: observational, experimental, simulation, and derived. The type of research data you collect may affect the way you manage that data. For example, data that is hard or impossible to replace (e.g., the recording of an event at a specific time and place) requires extra backup procedures to reduce the risk of data loss. Or, if you will need to combine data points from different sources, you will need to follow best practices to prevent data corruption.

#### **Observational Data**

Observational data are captured through observation of a behaviour or activity. It is collected using methods such as human observation, open-ended surveys, or the use of an instrument or sensor to monitor and record information -- such as the use of sensors to observe noise levels at the Mpls/St Paul airport. Because observational data are captured in real time, it would be very difficult or impossible to re-create if lost.

#### **Experimental Data**

Experimental data are collected through active intervention by the researcher to produce and measure change or to create difference when a variable is altered. Experimental data typically allows the researcher to determine a causal relationship and is typically projectable to a larger population. This type of data is often reproducible, but it often can be expensive to do so.

#### **Simulation Data**

Simulation data are generated by imitating the operation of a real-world process or system over time using computer test models. For example, to predict weather conditions, economic models, chemical reactions, or seismic activity. This method is used to try to determine what would, or could, happen under certain conditions. The test model used is often

as, or even more, important than the data generated from the simulation.

#### **Derived / Compiled Data**

Derived data involves using existing data points, often from different data sources, to create new data through some sort of transformation, such as an arithmetic formula or aggregation. For example, combining area and population data from the Twin Cities metro area to create population density data. While this type of data can usually be replaced if lost, it may be very time-consuming (and possibly expensive) to do so.

#### **Procedure of data analysis**

Data analysis method follows the procedures listed under the following sections. The data analysis part answered the basic questions raised in the problem statement. The detailed analysis of the developed and developing countries' experiences on OSH regarding manufacturing industries was analysed, discussed, compared and contrasted, and synthesized.

#### **Quantitative data analysis**

Quantitative data were obtained from primary and secondary data discussed above in this chapter. This data analysis was based on their data type using Excel, Office Word format, and other tools. This data analysis focuses on numerical/quantitative data analysis.

Before analysis, data coding of responses and analysis were made. In order to analyse the data obtained easily; the data were coded to SPSS 20.0 software as the data obtained from questionnaires. This task involved identifying, classifying, and assigning a numeric or character symbol to data, which was done in only one way pre-coded. In this study, all of the responses were pre-coded. This process was applied to every earlier question that needed this treatment. Upon completion, the data were then entered to a statistical analysis software package, SPSS version 20.0 on Windows 10 for the next steps.

Under the data analysis, exploration of data has been made with descriptive statistics and graphical analysis. The analysis included exploring the relationship between variables and comparing groups how they affect each

other. This has been done using cross tabulation/chi square, correlation, and factor analysis and using nonparametric statistic.

### Qualitative data analysis

Qualitative data analysis used for triangulation of the quantitative data analysis. The interview, observation, and report records were used to support the findings. The analysis has been incorporated with the quantitative discussion results in the data analysis parts.

### Data analysis software

The analysis supported with SPSS software much contributed to the finding. It had contributed to the data validation and correctness of the SPSS results. The software analysed and compared the results of different variables used in the research questionnaires. Excel is also used to draw the pictures and calculate some analytical solutions.

## RESULT AND DISCUSSION

- Vitamin D deficiency is one of the most prevalent disorders among mothers and children. Although in the past few decades, early diagnosis of vitamin-D deficiency and availability of supplementations and treatment modalities have improved the deficiency condition; hypovitaminosis D still exists as a major public health concern associated with significant morbidities in a variety of countries. Unfortunately, among Iranian women who have sunlight exposure deprivation and inadequate dietary vitamin D intake, it is highly prevalent. Reports indicate that 80% of old people of that old age home. Also, newborns suffer from vitamin D deficiency.
- This calls for appropriate and concrete public health action. The following measures can be taken to reduce the burden of the disease.
- Food fortification with Vitamin D is the best option to address this issue. All grades of milk can be fortified. Oil and milk products such as curd, yogurt, infant formulas, and butter can be fortified with Vitamin D. Widely consumed food items such as atta, Maida, and rice flour can also

be fortified. Vitamin D fortified food items should be made available to the public at minimal cost and be included in the public distribution system. Effective legislation is required to ensure this. Sustained political and administrative will and support are a must for the development of a fortification program. In India, Vanaspati (dalda) is fortified with 200 IU of Vitamin D per 100 g. Milk products of certain brand are also fortified with Vitamin D.

- Educational programs are a must to create awareness about Vitamin D deficiency as it is the most underdiagnosed and undertreated nutritional disease. Both physicians and the public should be made aware of its implications. To develop, launch and sustain such a program, adequate investment in the form of time, money, and effort is required.
- Vitamin D supplements of good quality should be made available at PHC level for the population at risk, i.e., pregnant women, lactating women, children, and elderly.
- Revision of RDA for Vitamin D by ICMR is needed as it is less compared to other guidelines.
- School going children can be benefitted from the following: educating them about the need for Vitamin D sufficiency and healthy lifestyle; providing Vitamin D fortified foods at mid-day meals in schools; daily physical exercise which would ensure exposure to sunlight.
- Testing facilities for Vitamin D levels should be made affordable and accessible to those at high risk of clinical Vitamin D deficiency (pregnant women, children, elderly especially women), as mass screening is not feasible.
- Government should support research groups to study and monitor the impact of supplementation programs and fortification strategies.

### Safety Considerations

It has been suggested that vitamin D supplementation can safely be utilized in early old age. Furthermore, our study participants

who received treatment had vitamin D deficiency and hence, the risk of hypervitaminosis D was reduced to almost zero. Also, during the screening program, any medical condition or probable side effects of vitamin D detected were promptly recorded and discussed by a qualified medical specialist involved in the study.

### CONCLUSION

Widespread prevalence of vitamin D deficiency in India is undeniable. Factually, sun exposure is an untenable solution, for most individuals in India, towards attaining vitamin D sufficiency. Low calcium intake in conjunction with vitamin D deficiency makes matters worse. The need for improvement in vitamin status of the Indian population is both important and urgent. The Indian government needs to take substantive measures in this direction. Revision of RDA for calcium and vitamin D is required. Better facilities and technologies should be made available countrywide to enable timely diagnosis of clinical manifestations of vitamin D deficiency in individuals who need attention by the clinicians. Population-based programs at the national level must be developed to increase awareness of the problem at hand, to provide affordable vitamin D supplements and also to provide vitamin D fortified foods to the Indian populace at large. Research in this field needs continued support to provide a comprehensive picture of the ongoing vitamin D problem and also to study and monitor the effect (s) of a partnership between the government, healthcare system, industry and consumers, aimed at improving the vitamin D status in India.

Vitamin D and calcium are important in the mechanical and structural integrity of the skeleton. Subclinical vitamin D deficiency (vitamin D insufficiency) is common in the fit, active elderly population and leads to an amplification of age-related bone turn over, bone loss and thus increased risk of fracture, mediated by secondary hyperparathyroidism. Daily supplementation with vitamin D can reduce the secondary hyperparathyroidism and

increase bone marrow density but only combination calcium and vitamin D therapy has been shown to be effective in reducing non-vertebral fractures. In order to maintain a “good bone health” guidelines concerning the recommended dietary intakes should be followed. Although many controversies still exist, normal serum Vit. D levels are recommended.

A screening for Vit. D deficiency in individuals at risk for deficiency is required and the appropriate treatment is recommended keeping in mind that more vitamin D is not necessarily better. The beneficial role of Vit. D in prevention of conditions such as osteoarthritis and stress fractures remain to be seen.

### CONCLUSIONS AND TAKE HOME MESSAGES

1. Patients with SLE (Systemic lupus erythematosus) are more prone to be vitamin D deficient compared to the general population; however, vitamin D deficiency is common also in healthy individuals.
2. Potential determinants of vitamin D deficiency in SLE include reduced UV exposure, genetic variations, corticosteroid treatment, and renal disease.
3. Current knowledge is not conclusive with regards to the role of vitamin D deficiency in the development of autoimmunity and, specifically, SLE. Increased risk of SLE associates with polymorphisms of the VDR; higher incidence of vitamin D deficiency.
4. Numerous observational studies have investigated the correlation between vitamin D levels and clinical/serological manifestations of lupus with contrasting results. A negative relationship between vitamin D levels and disease activity, renal disease, CV risk factors and complications, fatigue, and anti-dsDNA titres have been described but not conclusively accepted.
5. Several interventional studies have tried to define the therapeutic value of vitamin D supplementation on disease activity, renal



function, CV risk, fatigue, immunological profiles, and IFN-signature, however, once again, drawing controversial conclusions. Further large clinical trials with well-defined therapeutic protocols and goals are warranted to shed light on this topic.

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