

SUBOPTIMAL VITAMIN D STATUS IN INFANTS BETWEEN 1 AND 24 MONTHS OF AGE

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ABSTRACT

Introduction. Vitamin D is well known for its role in calcium absorption and maintenance of healthy bones and its deficiency results in rickets. Serum 25-hydroxyVitamin D (25(OH) D) is the most abundant Vitamin D metabolite and its concentration reflects Vitamin D status in humans. The aim of this study was to analyse the level of 25(OH) D in children between 1 month and 24 months of age, admitted in Sibiu Children's Hospital, with various pathologies, and to give scientific evidence for the prevention and treatment of rickets.

Materials and methods. We made a retrospective study on 200 children, aged between 1 month and 24 months, hospitalized in different Pediatric Departments of Sibiu Children's Hospital between 01.09.2015 and 01.11.2016, in whom we determined the level of serum 25(OH)D. The optimal level of 25(OH)D was considered to be ≥ 30 ng/ml; values of 25(OH) D between 20-29 ng/mL define insufficient Vitamin D and Vitamin D deficiency is characterized by levels < 20 ng/ml.

Results. Overall, 111 children (55.5%), aged between 1 month and 24 months, had levels of 25 (OH) Vitamin D below 30 ng/ml, with a mean value of 28.68 ng/ml. Of these 111 patients, 87 (78%) had 25(OH)D values between 20-29 ng/ml, with a mean value of 22.61 ng/ml and only 24 children (22%) had values less 20 ng/ml, with a mean value of 17.2 ng/ml.

Conclusions. Low serum 25(OH) D levels affect more than half of infants and children, aged 1 month to 24 months, suggesting that there are many children in our area who have suboptimal levels of Vitamin D and this should be a matter of concern for families with children, for medical professionals and public health authorities. Determination of 25(OH) Vitamin D is an important test for children between 1 month and 24 months of age, to be used as a starting point in efficiently preventing rickets at this age.

Keywords: Vitamin D deficiency, 25-hydroxyVitamin D, children, rickets

INTRODUCTION

Vitamin D is called the sunshine vitamin. Historically, in children, Vitamin D is well known for its role in calcium absorption and maintenance of healthy bones and its deficiency results in rickets. Nutritional or classical "rickets" is a worldwide disease involving mostly infants and young children having inadequate sunlight exposure, often associated with a low dietary intake of Vitamin D. Rickets is no longer considered a disease of the past or a disease that is limited to low-income countries (1). There are many explanations in the last years about the deficiency of Vitamin D and its relation to new lifestyle: less sunlight exposure, indoor living, dietary choices (2).

In order to prevent rickets, many countries apply Vitamin D supplementation strategies in infants, but the guidelines are not based on scientific evidence because it is only recently that Vitamin D status can be measured. Serum 25-hydroxyVitamin D (25OHD) is the most abundant Vitamin D metabolite and its concentration reflects Vitamin D status in humans.

Optimal Vitamin D status has been defined based on this Vitamin's effect on bone health (3). There are many debates about what Vitamin D deficiency really is. The Institute of Medicine and the American Academy of Pediatrics define Vitamin D deficiency when the 25 OHD level is lower than 20 ng/ml, Vitamin D insufficiency when 25 OHD lev-

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els fluctuate between 20 and 29 ng/ml, and Vitamin D sufficiency when 25 OHD levels reach or overtake 30 ng/ml.(4).

Is Vitamin D deficiency a problem in Romania? Vitamin D status in Romania is unreported mainly because Vitamin D determination is not a usual laboratory test because it is expensive and is not reimbursed by the National Insurance House.

Because worldwide, Vitamin D deficiency seems to be a real public health problem (in USA, studies show that 25% to 57% of American adults and adolescents are Vitamin D deficient, in India, Lebanon, Saudi Arabia, Turkey and the United Arab Emirates, 30 to 50% of adults and children have Vitamin D deficiency (5), we aimed at comparing our children population values with the literature and give a scientific evidence to this health problem.

The aim of this study was to analyse the level of 25 hidroxyVitamin D in children between 1 month and 24 months of age, admitted in Sibiu Children’s Hospital, with various pathologies, and to give scientific evidence for the prevention and treatment of rickets.

MATERIALS AND METHODS

We made a retrospective study on 200 children, aged between 1 month and 24 months, hospitalized in the Pediatric Departments of Sibiu Children’s Hospital, between 01.09.2015 and 01.11.2016 and we analysed the results of the 25(OH)D levels. For the study, we used the results from the electronic archives of the hospital.

Serum 25(OH) D levels were measured by an automated ELFA-based assay, Vidas PC analyzer (BioMerieux, France), using BioMerieux reagents, in the central laboratory within the Children’s Hospital (Sibiu, Romania). This assay employs a competitive test principle using recombinant Vitamin D binding protein allowing measurement of both 25(OH)D₂ and 25(OH)D₃, instead of using a monoclonal antibody against 25(OH)D.

Blood samples were centrifuged promptly and serum samples were stored frozen in aliquots until

analysis. The stored samples were then sent to the laboratory for measurement of serum 25(OH) D at the same time.

We considered the 25OHD optimal level, values ≥30 ng/ml, insufficient Vitamin D, the levels between 20 and 29 ng/ml and deficient Vitamin D, the levels < 20 ng/ml.

STATISTICAL ANALYSIS

All data analyses were performed using the SPSS statistical package version 15.0 for Windows (SPSS, Chicago, IL, USA). A P-value < 0.05 was considered statistically significant. We categorized serum 25(OH)D levels in 3 distinct categories: ≥30 ng/mL, between 20 and 30 ng/mL, < 20 ng/mL.

RESULTS

Among the 200 children tested, aged between 1 month and 24 months, 111 children (55.5%), had levels of 25 (OH) Vitamin D below 30 ng/ml, with the group average of 28.68 ng/ml (SD 4.2) (Fig. 1).

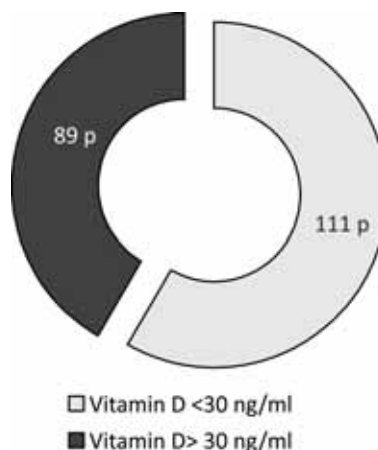


FIGURE 1. Plasmatic Vitamin D levels

Among these 111 patients, 87 (78%) had 25OHD values between 20 and 29 ng/ml, with the group average of 22.61 ng/ml (SD 4.1), and only 24 children (22%) had values less than 20 ng/ml, with the group average of 17.2 ng/ml (SD 4.1) (Fig. 2).

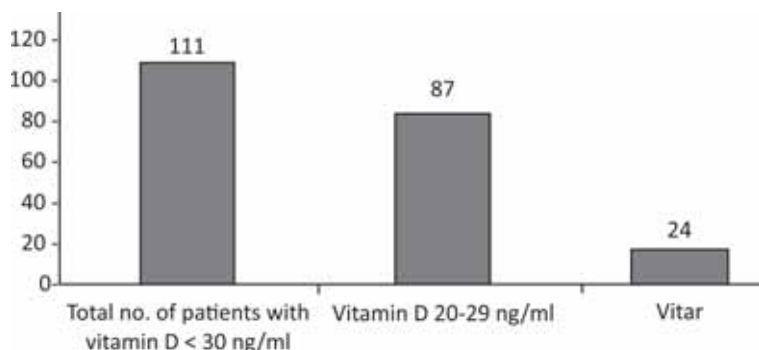


FIGURE 2. Vitamin D – low levels distribution

DISCUSSIONS

Vitamin D is the sunshine vitamin. During exposure to sunlight 7-dehydrocholesterol in the skin absorbs the UV radiation and is converted to preVitamin D₃. The preVitamin D₃ isomerizes into Vitamin D₃. PreVitamin D₃ and Vitamin D₃ also absorb the UV radiation and are converted into a variety of photoproducts with different biologic properties. The Vitamin D synthesis is sun dependent and, consequently, is very much influenced by season, time of day, latitude, altitude, air pollution, skin pigmentation, sunscreen use, passing through glass and plastic and aging. After the its production, Vitamin D is metabolized in the liver and kidneys into 25-hydroxyVitamin D which is a major circulating form and 1.25-dihydroxyVitamin D, which is the biologically active form. 1.25-dihydroxyVitamin D plays an important part in regulating calcium and phosphate metabolism for the maintenance of metabolic functions and for skeletal health. Most cells and organs in the body have a Vitamin D receptor and many cells and organs are able to produce 1.25-dihydroxyVitamin D. As a result, 1.25-dihydroxyVitamin D influences a large number of biologic pathways, which may help explaining the association of Vitamin D in autoimmune diseases, some cancers, cardiovascular disease, infectious disease, type 2 diabetes, schizophrenia (6).

In the last years, with the help of laboratory techniques, we can measure the level of Vitamin D in serum and many countries reported high prevalence of low levels of Vitamin D, known as Vitamin D deficiency (levels of 25-OHD < 20 ng/ml) or Vitamin D insufficiency (levels between 20-29 ng/ml).

The main reasons for low levels of Vitamin D are (7):

- Lack of Vitamin D in the diet, often in conjunction with inadequate sun exposure
- Inability to absorb Vitamin D from the intestines
- Inability to process Vitamin D due to kidney or liver disease

Infants and children are at risk for low Vitamin D levels because human breast milk contains low levels of Vitamin D and most infant formulas do not contain adequate Vitamin D (8).

Parents of infants and children are often advised to keep their child out of the sun, which reduces Vitamin D synthesis from the skin (9).

Certain diseases affect the body's ability to absorb adequate amounts of Vitamin D through the intestinal tract. Examples of these include celiac

disease, Crohn's disease, and cystic fibrosis that are diagnosed in this period of life (10).

The liver and kidney have important enzymes that change Vitamin D from sun-exposed skin or food to the biologically active form of Vitamin D. People with chronic kidney and liver disease are at increased risk of low active Vitamin D levels because they have decreased levels of these enzymes (11).

Less common causes of Vitamin D deficiency include familial diseases that impair the enzymes in the liver or kidney that create the biologically active form of the Vitamin. This results in inadequate amounts of active Vitamin D.

Vitamin D was first known to have a role in calcium absorption and maintenance of healthy bones, and the first disease associated to Vitamin D deficiency was rickets (12). The year 1645 is commonly recognized as the opening year for the scientific literature on rickets because David Whistler (1619–1684) described the disease in his M.D. thesis at the University of Leiden, the Netherlands, with the title “*De morbo puerile anglorum, quem patrio idiomate indigenae vocant the Rickets*” (Concerning the disease of English children, which in English it is called “Rickets”).

Many years, the disease has been diagnosed using only clinical and radiological parameters because there was no analytical method to determine Vitamin D. At present, the best indicator of Vitamin D status is the serum 25(OH)D.

Although, there is no universally accepted consensus yet on serum 25(OH)D thresholds to define optimal Vitamin D status, Vitamin D deficiency is defined by most experts as <20 ng/mL, and insufficiency as <30 ng/mL, with threshold values based on optimal bone health (13).

In the current study, these cut-offs were applied to children aged 1 month -24 months, and we found a high number of children, 111 patients (55.5%), with insufficient Vitamin D levels, and only 24 children (22%) with sufficient Vitamin D (levels <20 ng/ml).

Comparing our results with an Asian study where Vitamin D insufficiency (defined as serum 25(OH)D <30 ng/mL) was found in 90.3% and Vitamin D deficiency (defined as serum 25(OH)D <20 ng/mL) was found in 51.0%, we can conclude that there is a lot of variability in Vitamin D deficiency around the world (14).

Our study has some limitations: the determination of 25OHD was made in autumn; the deficiency prevalence can be lower because it was after the summer season, when levels of Vitamin D increase,

after sun exposure. We have to continue our research in spring, after the winter season, with less sun exposure in our geographical area.

This study has a notable strength: it is a first research on children Vitamin D levels in our area, and gives us an idea of the phenomenon and the results have to be known by the medical professionals, to correctly evaluate the incidence of Vitamin D deficiency in children. The rickets prevention and treatment can benefit from this determination because it offers a scientific evidence of the disease and can be a good starting point for further determinations.

CONCLUSIONS

Low serum 25(OH) D levels affect more than half of infants and children, between 1 month and 24 months, suggesting that there are many children in our area, who may have suboptimal levels of Vitamin D and, this should be a matter of concern for families with children, for medical professionals and public health authorities. Determination of 25(OH)vit D is an important test for children between 1 month and 24 months in order to implement an efficient rickets prevention at this age.

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