



## Risk Factors for Low Serum 25 OHD Concentrations in Healthy Infants in Algeria

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### Abstract

Knowledge of vitamin D has made great progress in recent years with the identification of its receptors (VDR) in most tissues, passing it from the role of a purely phosphocalcic and bone tropic hormone to that of a hormone playing a role global health.

In Algeria, we lack epidemiological studies to assess the vitamin D status of healthy and supplemented infants. Through this work, we propose to determine the vitamin D status, to assess the vitamin D nutritional intake of healthy infants and to identify risk factors related to hypovitaminosis D in order to target and treat populations at risk.

**Results:** The analysis covers 395 infants aged between 9 and 24 months recruited during the 4 seasons. The mean age was

11.5 ± 1.3 months. The sex ratio was 1.5. The average daily dietary intake of vitamin D was estimated at 167 IU/d (4.1µg/d). 90% of the children had low daily food intakes (less than 200IU/d).

The mean total vitamin D level in our series was 15.6 ± 4.4 ng/ml, significantly lower than current recommendations (25 OHD > 20 ng/ml) with a mean PTH level of 38 ± 4.2 pg/ml.

The prevalence of vitamin D deficiency increased from 50% in the 12-24 month age group, to 75% in the 09-12 month group in winter, and from 21% in children aged between 12 and 24 months to 64% in children aged between 09.

The risk of vitamin D deficiency is associated with individual factors that cannot be modified (skin pigmentation), lifestyle habits (lack of sunlight, insufficient dietary intake of vitamin D and) and environmental factors (season).

**Conclusion:** The magnitude of the prevalence of hypovitaminosis D in infants with high bone growth velocity and increased vitamin D requirements prompts us to question vitamin D drug supplementation. Six-monthly systematic vitamin D supplementation would be necessary for children with risk factors as well as children without risk factors in the winter period according to the results of our study.

**Keywords:** 25 OHD; Vitamin D Intake; Infants; PTH; Algeria

## Introduction

Knowledge of vitamin D has made great progress in recent years with the identification of its receptors (VDR) in most tissues, shifting it from the role of a purely phosphocalcic and bone tropism hormone (primary role in maintaining vitamin D), phosphocalcic homeostasis, bone mineralization and prevention of rickets) to that of a hormone playing an overall role in health [1]. Many studies suggest its role in protection against infectious pathologies (tuberculosis, viral infections), autoimmune (type I diabetes).

Most epidemiological studies in Europe, the United States and Asia show that vitamin D deficiency and insufficiency are very common and underdiagnosed, not only in elderly populations with chronic pathologies but also in adult populations and healthy pediatrics. Whatever the threshold used, the prevalence of vitamin D insufficiency is estimated between 30 to 80% in different populations and under various latitudes [2-4].

The prevention strategy currently followed seems satisfactory, insofar as we observe practically no more deficiency rickets in our country, however there are very few studies concerning the evaluation of the vitamin D status in healthy infants in Algeria.

We lack in Algeria epidemiological studies to assess the vitamin D status of healthy infants and supplemented yet the latter with a significant growth rate deserves special attention in order not only to avoid the deficiency but to seek optimization.

We propose through this work, to determine the vitamin D status, to assess the vitamin D nutritional intake of healthy infants and to identify the risk factors related to hypovitaminosis D in order to target and treat at-risk populations in the commune. by Hussein dey.

The commune of Hussein Dey is located east of the wilaya of Algiers (capital of the country), has for geographical coordinates a latitude at 36° 44' 39" North and a longitude at 3° 5' 31" East.

The commune of Hussein Dey faces the bay of Algiers culminating at 9 meters above sea level and covers an area of 5 km<sup>2</sup>. The climate is Mediterranean with an average annual sunshine duration of 2700 hours. August is the hottest month of the year with an average temperature of 25.5°C and January the coldest month of the year. The average temperature is 11.8°C at this time.

Our study is a cross-sectional, prospective, descriptive, analytical and unicentric study. The inclusion of healthy infants was done chronologically and consecutively during all the months of the year. The duration of the study was two years, from January 1, 2017, to December 31, 2019, conducted during the 4 seasons.

The sample was formed according to a random survey by simple draw by numbering (statistical method validated by the WHO). Recruitment was carried out chronologically and consecutively with a similar workforce during the 4 seasons. The choice of children to be drawn by lot was made according to their number on the day of the consultation after having obtained the written and signed consent of the parents.

Taking these data into account, we have included the - Healthy infants aged 9 to 24 months.

- Vitamin D received at 1 and 6 months according to the national scheme (after checking the health record).
- Free of any chronic or acute pathology that may interfere with the metabolism of vitamin D (Skin, digestive, hepatic, parathyroid and renal pathology, etc.).
- Not receiving any treatment with vitamin D or calcium in the 3 months preceding inclusion.
- Not receiving any treatment that may interfere with vitamin D metabolism or calcium phosphate metabolism: Anticonvulsants, corticosteroids, rifampicin....

An information sheet was drawn up comprising several items. This questionnaire made it possible to provide information on age, sex, height and weight measurements and skin pigmentation according to a color chart (international classification by Fitzpatrick) [5]. For the dietary survey, the parents of infants had to answer an exhaustive questionnaire concerning their child's vitamin D intake: frequency, type and quantity of food consumed during the week preceding the survey.

The determination of total 25OHD was carried out on serum after centrifugation by the VIDAS BioMérieux analyzer which allows the immunoenzymatic determination of 25OHD by ELFA technique (Enzyme Linked fluorescent Assay). The vitamin D standards used for the evaluation of our results are those accepted by the majority

of authors, set by the American Society of Endocrinology and the GRIO [6] (Standards applied by our laboratory). The PTH assay was performed by the Cobas e411 Roche diagnostic analyzer. The biochemistry unit carries out daily internal quality control before any validation of the results. The acceptable coefficients of variation in the laboratory are less than 3% of the recommended target regardless of the measured parameter.

SPSS 22 software was used for statistical analysis. First, we carried out a descriptive analysis of the study population. In a second step, a univariate analysis was carried out in order to determine which factors could be influencing the variations in the 25(OH) vitamin D level of the patients included. The significance threshold of the statistical tests and the simple logistic regression and multiple is  $p < 0.05$ .

## Results

The analysis covers 395 infants aged between 9 and 24 months recruited during the 4 seasons. The mean age was  $11.5 \pm 1.3$  months. The sex ratio was 1.5.

We adopted the Fitzpatrick scale which classifies skin pigmentation into 6 phototypes to assess the phototype of our series. Fair complexion was found in 40% of cases (Phototype I-III). More than a third of the children had a dull complexion (Phototype IV), i.e., 35%. 21.4% of the children had a brown complexion (Phototype V) and only 6 children or 0.6% had a black complexion (Phototype VI).

The evaluation of dietary intakes of vitamin D is difficult to carry out, there is currently no self-questionnaire to correctly estimate the exogenous intake of vitamin D.

The questionnaire adopted is mainly based on the Ciquel table [7] which allows the estimation of dietary vitamin D intake from a dietary survey based on the consumption of milk and other dairy products (yogurt, cheese, butter and margarine), oily fish and eggs.

The vast majority of children (60%) had dietary intakes of vitamin D between 100 and 200 IU/d. Only 5% of the children had a daily dietary intake of vitamin D greater than 200 IU/day. 90% of the children had low daily food intakes (less than 200IU/d).

65% of these children consumed ordinary reconstituted milk, 7% reconstituted canned milk enriched with vitamin D as for dairy

products, 55% consumed it 1 to 2 times per week, 35% consumed it 1 to 2 times per month. 81% of children ate at least one food naturally containing vitamin D per week.

The average daily dietary intake of vitamin D was estimated at 167 IU/day ( $4.1 \mu\text{g/day}$ ) with a median of 152 IU/day ( $3.75 \mu\text{g/day}$ ) and extremes between 70 and 240 IU/day ( $1.75\text{-}5.75 \mu\text{g/day}$ ). The mean total vitamin D level in our series was  $15.6 \pm 4.4 \text{ ng/ml}$ , significantly lower than current recommendations ( $25 \text{ OHD} > 20 \text{ ng/ml}$ ) with a mean PTH level of  $58 \pm 4.2 \text{ pg/ml}$ .

The prevalence of vitamin D deficiency increased from 50% in the 12-24-month age group, to 75% in the 09-12-month group in winter, and 21% in children aged between 12 and 24 months to 54% in children aged between 09 and 12 months in summer. The risk of vitamin D deficiency is associated with individual factors that cannot be easily modified (pigmentation of the skin), lifestyle habits (lack of sunshine, insufficient dietary intake of vitamin D and) environmental factors (season). summary of the results of the determinants of hypovitaminosis D by univariate and multivariate analysis are reported in table A.

## Discussion

The diversity of the populations studied, particularly in terms of latitude, geographical origin or age, the variability of the assay techniques and the absence of any real consensus on the reference thresholds for defining the deficit make international comparisons difficult. However, an increase in vitamin D deficiency has been observed at all latitudes and on all continents.

Vitamin D deficiency appears to be a major public health problem in both developed and developing countries. No study has been conducted either in the Maghreb or in Algeria concerning healthy infants, however, this population at a significant growth that deserves special attention.

In our series, there was a statistically significant inverse correlation ( $p = 0.01$ ) between age and the prevalence of vitamin D deficiency, namely that the younger the child, the higher the prevalence of vitamin D deficiency. Thus, the prevalence of vitamin D deficiency increased from 50% in the age group of 12-24 months, to 75% in the age group of 09-12 months in winter, and from 21% in children aged between 12 and 24 months at 64% in children aged

Risk factors	Terms	UNI VARIOUS ANALYSIS				Multivariate analysis		
		% Deficit Vit D	Raw GOLD	95% CI	P	OR adjusted	95% CI	P
Age	09- 12 months	70.9	4.8	4-5.6	< 10 <sup>-5</sup>	3.8	3.4-4.4	0.0001
	12-24 months	46.5	1					
Phototype	IV-VI	79.5	6.4	4.8-8.4	< 10 <sup>-5</sup>	2.8	2.2-5.2	0.001
	I-III	37.9	1					
CSE	Poor	91.4	3.5	2.6-5	0.006	3.9	1.5-4.3	0.01
	Fair/Good	55.6	1					
Contributions dietary vitamin D	< 200 IU	74.4	3.6	2.5-5.2	0.005	2.6	1.6-4.2	0.02
	> 200 IU	40.5	1					
Season	Winter autumn	84.8	8.8	5.5-14	< 10 <sup>-5</sup>	7	3-11	0.001
	Summer /Spring	38.7	1					

**Table A:** Multivariate analysis of the determinants of hypovitaminosis D by multiple logistic regression.

between 09 and 12 months in summer. This is probably due to a greater sun exposure of the 12-24 month age group compared to children aged between 09 and 12 months.

Many studies have been carried out in adolescents but very few in infants. Among these studies, the one carried out in infants aged 8 to 10 months in 10 French cities from 1988 to 1990 [8] showed that 50% of children had levels below 12 ng/ml. These results led to an enrichment of 1992 infant milks with vitamins and since 2004 oils have been enriched with vitamin D This enrichment was quickly followed by a collapse in the prevalence of deficiency rickets (69 cases in 1991 to 1 case in 2005).

Gordon., *et al.* in 2009, found in 365 infants a vitamin D level below 30 ng/ml in 40% of these children, 12% had a vitamin D concentration below 20 ng/ml; a third of the latter having radiological signs of rickets [9].

In Turkey; an evaluation of vitamin D deficiency and insufficiency was carried out between January 2008 and January 2010 by the pediatric endocrinology department of Ankara University Hospital by Nesib in 440 children aged 0 to 16 years. 25% of these children had a vitamin D level below 20 and 15% had a level below 30 ng/

ml [10].

In Algeria; During the 1960s, deficiency rickets was an important cause of morbidity and mortality, in particular because of its respiratory complications. Rickets was observed in one in three children under the age of 3 in national surveys carried out in 1963 and 1965. In 1973, Si Ahmed [11] noted a radiological incidence of rickets of 33% in children aged 3 at 23 months. A year later Chouakri [12] found an incidence of 49%, in the same age group at the level of the city of Fougeroux (Bouzareah).

From independence, among the prevention strategies adopted, the most important was to administer 1 vial of 200,000 IU of vitamin D at 1, 6, 12, and 18 months. Ministerial instruction 841 of December 21, 1998, fixes at the age of 1 and 6 months, the systematic intake of a dose of 200,000 IU, to fight against rickets.

In 1984 and 1985 in Constantine, H. Benmokhbi [13] observed that 18.7% of infants supplemented according to the national scheme were suffering from deficiency rickets, moreover she noted that the level of 25 OHD tended to decrease four months after taking vitamin D.

The phototype was an important determinant of hypovitaminosis D since the darker the skin, the lower the vitamin D level (mean vitamin D level was  $22 \pm 12$  ng/ml for the light phototype vs  $14.5 \pm 10$  ng/ml for the dark phototype in our study) with a risk of hypovitaminosis D multiplied by 2.8 CI: 95% (2.2-5.2) for children with a dark phototype compared to those who had a light phototype (this risk increased from 2.8 in summer to 4.5 in winter). This difference has been highlighted in several studies which have shown that with an equal capacity for vitamin D synthesis by UVB rays, subjects with a dark phototype require a longer exposure time to produce the same quantity of vitamin D. In the American NHANES III study, the authors noted a significant difference between white, Hispanic and black children. African Americans were the most deficient with a prevalence of hypovitaminosis D of 35% [14].

Food provides small amounts of vitamin D unlike endogenous synthesis after adequate sun exposure providing more than 80% of the body's needs. The food survey questionnaire, although exhaustive and carried out with parents, is based on the parents' ability to quantify their child's diet.

over a given period, which is not easy given the different custody methods which may possibly induce a margin of error. However, it appears that the vast majority consume ordinary milk and therefore little milk enriched with vitamin D. In our study, the average daily dietary intake of vitamin D was estimated at 164 IU/d ( $4.1 \mu\text{g}/\text{d}$ ) with a median 150 IU/day ( $3.75 \mu\text{g}/\text{day}$ ) and extremes between 70 and 230 IU/day ( $1.75$ - $5.75 \mu\text{g}/\text{day}$ ).

Various studies around the world have found that dietary intakes of vitamin D are insufficient, which has led some governments to adopt a nutritional policy of fortifying certain commonly consumed foods with vitamin D. The INCA 2 survey conducted in France in 2007 among children aged between 3 and 17 noted that the children had a dietary intake of vitamin D of  $2 \mu\text{g}/\text{day}$  [15]. Weng in the USA had evaluated the daily dietary intake of vitamin D in 382 children aged 6 to 21 years, the daily intake of vitamin D below 200 IU/day was associated with a low vitamin D status: OR = 1.6 CI: 1.1 -2.5 ( $p = 0.0005$ ) [16].

## Conclusion

Our study conducted over the whole year allows us to draw a certain number of lessons as observed in other stud-

ies. The risk of vitamin D deficiency is associated with individual factors that cannot be modified (skin pigmentation), lifestyle habits (lack of sunlight, insufficient dietary intake of vitamin D and) and environmental factors (season). Our study also shows that the risk of vitamin D deficiency is frequent, especially at the end of winter. Although this deficit is generally not accompanied by clinical signs of rickets, it could however constitute a risk factor for modification of the density and structure of the bone tissue.

The detection and treatment of vitamin D deficiency is a public health issue, especially since recent publications show that vitamin D plays a role in many pathologies that go beyond phosphocalcic metabolism. The magnitude of the prevalence of hypovitaminosis D in infants with high bone growth velocity and increased vitamin D requirements prompts us to question vitamin D drug supplementation. Six-monthly systematic vitamin D supplementation would be necessary for children with risk factors as well as children without risk factors in the winter period according to the results of our study.

## Declaration of Interests

No conflict of interest.

## Bibliography

1. Cavalier E and JC Souberbielle. "Vitamin D: "classical" and "non-classical" effects and assessment of patient status Nuclear Medicine 33 (2009): 7-16.
2. Amstutz V., et al. "Vitamin D: news and recommendations". *Swiss Medical Review*.
3. Souberbielle JC., et al. "News on the effects of vitamin D and the evaluation of vitamin D status". *Revue Francaise des Laboratoires* 414 (2019): 31-38
4. Vidailhet M., et al. "Vitamin D: A vitamin Still relevant in children and adolescents. Nutrition Committee of the French Society of Pediatrics". *Archives of Pediatrics* 19 (2012): 316-328.
5. The Fitzpatrick Skin Type Classification Scale". *Skin Inc* (2014).
6. Winzenberg T and Powell S. "Effects of vitamin D supplementation on bone density in healthy children: systematic review and meta-analysis". *BMJ* 342 (2011): c7254.

7. Ciqual. Anses. fr: Version (2014).
8. Mallet E and Claude V. "Calcium and vitamin D status of pre-school children. About a survey carried out in the Rouen region". *Archives of Pediatrics* 12 (2005): 1797-1803.
9. Gordon CM and Feldman HA. "Prevalence of vitamin D deficiency among healthy infants and toddlers". *Arch pediatrician AdolescMed* 162 (2008): 505-512.
10. Nesibe A. "Vitamin D deficiency in children and adolescents". *Journal of Clinical Research in Pediatric Endocrinology* (2012): 25-29.
11. Ahmed SR "Medico-social study of the Chéraga baldia infant". Doctoral thesis in medicine, Algiers (1974).
12. Chouakri O. "Study of the frequency of rickets in urban areas". Doctoral thesis in medicine, Algiers (1974).
13. Benmekhbi H. "Doctoral thesis in medical sciences, Constantine (1986).
14. Kumar T. "Prevalence and associations of 25OHD deficiency in US children: NHANES 2001- 2004". *Pediatrics* 124(2009):362-370.
15. French Food Safety Agency (Afssa). INCA2. National individual study of food consumption (2008).
16. Weng X. "Risk factors for low serum 25 OHD concentrations in otherwise healthy children and adolescents". *The American Journal of Clinical Nutrition* 86 (2007):150-158.