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Review Article

Vitamin D Deficiency in Brazil: Questions about Potential Causes and Clinical Characteristics*

Deficiência de vitamina D no Brasil: Questionamentos sobre as suas possíveis causas e características clínicas

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Abstract

Vitamin D is a micronutrient essential to various systems from the human body, and it is not restricted to the classical function of bone mineralization. Its synthesis is mainly related to ultraviolet B (UVB) radiation exposure. Although Brazil is a tropical country with high levels of UVB radiation, counter-intuitively, a large number of Brazilians present vitamin D deficiency, which is also a worldwide issue. This review aims to approach clinical features and explore potential causes for this apparent contradiction through questions that could explain vitamin D deficiency in the Brazilian population.

Keywords
- Vitamin D
- Avitaminosis
- Ultraviolet Rays

Resumo

A vitamina D corresponde a um micronutriente essencial ao funcionamento de diversos sistemas do corpo humano, não se restringindo à clássica função de mineralização óssea. A sua síntese está relacionada principalmente à exposição à radiação ultravioleta B (UVB). O Brasil é um país tropical que apresenta altos índices de UVB, no entanto, ao contrário do que se pode imaginar, observa-se um grande número de brasileiros deficientes em vitamina D e essa deficiência se torna um problema de ordem mundial. Essa revisão tem por objetivo abordar características clínicas e explorar as possíveis causas para essa aparente contradição, por meio de questionamentos que poderiam explicar a deficiência de vitamina D na população brasileira.

Palavras-chave
- Vitamina D
- Deficiência de Vitaminas
- Raios Ultravioleta

Introduction

Vitamin D is a fat-soluble steroid hormone, and it is considered a micronutrient essential to a complex endocrinological system.[1–6] Its action has been studied since the beginning of the 20th century and it is increasingly clear that vitamin D functions are not restricted to the classical bone mineralization regulation.[1–3,7]

Vitamin D has several roles, encompassing both endocrine reactions and functions from other systems, such as the immune system. Its protective immunomodulatory role in

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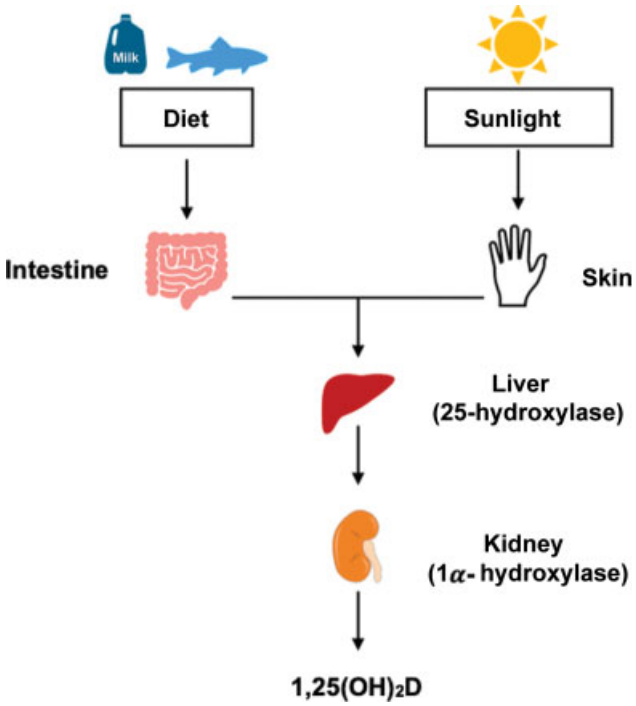

Fig. 1 Vitamin D metabolism. Source: Modified from "Alimentação, fotoexposição e suplementação: influência nos níveis séricos de vitamina D" (2015) and "Sunlight exposure: Do health benefits outweigh harm?" (2016).

conditions such as systemic arterial hypertension, cancer, osteoarthritis, multiple sclerosis, and diabetes mellitus is described.[1,2,8]

Although the main site of vitamin D metabolism (►**Figure 1**) is the skin, it also occurs in other properly functioning organs, such as the bowel, liver and kidney.[9,10] Cutaneous 7-dehydrocholesterol (pro-vitamin D3) is converted by ultraviolet B (UVB) radiation in cholecalciferol (vitamin D3), which can be also obtained from food sources.[9,10] Within the liver, an enzyme, called 25-hydroxylase, converts vitamin D3 in 25-hydroxy vitamin D3 (25 (OH) vitamin D) or calcidiol.[9,10] Calcidiol passes through the kidneys and undergoes a second hydroxylation by an enzyme called 1-alpha-hydroxylase, resulting on 1,25-dihydroxy-vitamin D3 (calcitriol), the active form of the molecule.[9,10] This enzyme is activated by parathyroid hormone and calcium and phosphate concentrations, demonstrating the close relationship between vitamin D and bone metabolism.[9,10]

Skin exposure to UVB radiation is the main source of vitamin D.[7,11,12] Vitamin D can be obtained from food, but with a lower efficiency compared to sunlight.[13,14] Vitamin D deficiency is a global health issue.[4,15] At first glance, it can be attributed to a reduction in UVB exposure, especially in countries with lower solar incidence.

However, tropical countries, such as Brazil, have a high UVB incidence and, despite the lack of populational studies, number of people with vitamin D deficiency is increasing.[16,17] This is curious given that UVB is the main source of vitamin D for the human body.[7,12,13]

Review

Data to effectively answer these questions were obtained from 57 sources describing the situation in Brazil, the United States, India, and France, showing that vitamin D, popularly known as the "sunshine vitamin,"[18] is extremely important and derived in different ways. UVB is the primary source of endogenously synthesized vitamin D, representing 80 to 90% of the daily fraction required by the body.[19,20] The spectrum of UVB radiation considered optimal for pre-vitamin D synthesis at the skin ranges from 290 to 320 nm; coincidentally, this is the same range associated with skin carcinogenesis.[21–23] In Brazil, the average daily UVB radiation ranges from 3,300 to 3,800 J/m^2, reaching values greater than 7,000 J/m^2 during the summer.[21,24] For people with light skin, very sensitive to the sun and with little pigmentation (phototype II), the exposure of small, uncovered skin areas for about 10 minutes is sufficient to absorb the required amount of UVB for vitamin D synthesis. In contrast, people with darker skin (phototype IV) would need a longer exposure time, since melanin absorbs UV radiation and limits the number of photons available for pre-vitamin D3 formation.[24]

Vitamin D-rich foods constitute a secondary source for this nutrient, accounting for 10% to 20% of the body requirements.[19] Therefore, vitamin D is rarely obtained in sufficient quantities with common diets.[25] The main sources of vitamin D3 are fatty fish from cold, deep waters, such as salmon and tuna.[19] Soy milk, margarine, breads, breakfast cereals, orange juice, and egg yolks are also good vitamin D sources.[1,10,26–28]

Brazil has a difficult ethnic classification due to its high degree of miscegenation.[29] As revealed by the 2016 National Continuous Household Sample Survey (PNAD), the Brazilian population is comprised of 8.2% black and 46.2% brown subjects. Thus, most Brazilians present higher phototypes, which could corroborate for the perceived vitamin D deficiency.

This hypovitaminosis usually occurs in obese individuals in a 50% higher proportion compared to eutrophic subjects.[30] This finding may be related to the presence of vitamin D receptors in the adipose tissue, which would extract the vitamin from the blood circulation, reducing its concentration. In addition, obesity tends to reduce sunlight exposure due to mobility limitations.[31,32]

It is estimated that approximately 80% of the world population live in areas with air pollution levels higher than those defined by air quality guidelines.[33,34] In Brazil, 75% of the population live in urban centers, where air pollution is a reality, especially in large cities. Thus, people from large Brazilian industrial centers potentially present higher rates of vitamin D deficiency.[11]

Serum vitamin D level is assessed by measuring the fraction of 25 (OH) vitamin D using mass spectrometry (considered the golden standard method).[7] This choice is based on the fact that calcidiol is the main metabolite in the bloodstream when compared to the active form of the vitamin. Vitamin D deficiency, insufficiency, and sufficiency are based on 25 (OH) vitamin D levels (►**Table 1**).[35–38]

Table 1 Reference values for 25 (OH) vitamin D according to the US Endocrine Society

Definition	Reference Values*
Sufficiency	30 to 100 ng/mL
Insufficiency	20 to 29 ng/mL
Deficiency	Lower than 20 ng/mL

*Reference values for 25 (OH) vitamin D
Source: Adapted from "Recomendações da Sociedade Brasileira de Endocrinologia e Metabologia (SBEM) para o diagnóstico e tratamento de hipovitaminose D" (2014).

What are the main risk groups for vitamin D deficiency?

Premature children; newborns exclusively receiving breast milk, which has a low amount of vitamin D; obese subjects; elderly people; pregnant women; patients with rickets/osteomalacia and osteoporosis; patients with a history of fall and fracture due to a deficiency which impairs muscle relaxation and contraction, resulting in pain and weakness;[39] subjects with hyperparathyroidism; inflammatory diseases; autoimmune diseases, such as multiple sclerosis, asthma and rheumatoid arthritis;[40,41] chronic kidney disease; and malabsorption syndromes.[42]

What is the clinical picture of vitamin D deficiency?

When vitamin D deficiency is not asymptomatic, patients may report irritability, sweating and even more severe conditions, such as rickets in children and osteomalacia in adolescents and adults. These more severe conditions result from hypocalcemia and hypophosphatemia, respectively caused by a reduced calcium and phosphate absorption and an increased phosphate clearance at the intestinal level.[39]

Are Brazilians not exposed to sunlight enough?

Lifestyle changed in recent years, especially regarding sunlight exposure. During the last century, Brazil has undergone an intense process of urbanization and economic development. An essentially rural population started to concentrate in cities. In urban centers, work is carried out basically indoors. There was also a reduction in outdoor physical activity and an increase in sedentary lifestyle, resulting in obesity.[43–46]

In addition, sunscreen use has become widespread. At first, it was assumed that sunscreens were responsible for vitamin D levels reduction both in the Brazilian and global populations.[24] Indeed, these products are effective in preventing UVB penetration into the skin. However, it is worth mentioning that sunscreens only provide the UVB protection indicated on the label when applied in an amount of 2 mg/cm^2 every two hours.[24] Routinely, few people use sunscreens properly to be fully protected from UVB radiation.

Data show that sunlight exposure of Brazilian people was reduced, either due to socioeconomic changes or to the increased use of sunscreens. However, the incidence of UVB in the country is high and the amount of UVB required for vitamin D synthesis is low, which calls into question this hypothesis as the only cause for the hypovitaminosis D seen in Brazil.

Is the Brazilian diet low in vitamin D?

The daily requirement for vitamin D is 1,500 to 2,000 IU/day (37.5 to 50 µg) for healthy adults.[10] It is unlikely that this dose is obtained from diet alone, even when foods with a very high content of vitamin D, such as those shown in ►**Table 2**, are consumed.

It is difficult to obtain enough vitamin D only from food in Brazil, since the basic local diet consists of items with a high nutritional content (rice, beans, milk, meat, and fruits), but with a low vitamin D index.[47] Thus, although the Brazilian diet can contribute to this hypovitaminosis, it is not its main cause, since foods are secondary sources.

Could Brazilian population miscegenation result in a reduced vitamin D synthesis?

Skin pigmentation affects the cutaneous synthesis of vitamin D. Therefore, people with a higher concentration of melanin present lower vitamin D synthesis because the pigment acts as a natural sunscreen, reducing UVB absorption.[16,46]

However, it is worth mentioning that such data are self-reported. In addition, there is a lack of studies linking miscegenation to vitamin D deficiency.

Could the increase in obesity in the Brazilian population interfere with vitamin D levels?

Obesity is a current worldwide public health problem. Data from the World Health Organization (WHO) revealed that, in 2016, more than 1.9 billion adults, aged 18 years old or over, were overweight, including more than 650 million obese subjects.[48] In Brazil, the situation is similar, and it is

Table 2 Main vitamin D-rich foods: note that few are commonly included in the Brazilian diet

Food	Portion size	Vitamin D (UI)
Fish liver oil	23.1 mg/ 1 tablespoon	924
Grilled salmon	100 g	284
Grilled mackerel	100 g	352
Canned tuna in brine	100 g	144
Canned sardine in brine	100 g	184
Chicken egg	50g/ 1 regular unit	3
Fried beef liver	100g	36
Fortified margarine	20g	62
Fortified breakfast cereal	30g/medium-sized portion	52

Source: Modified from "Funções Plenamente Reconhecidas de Nutrientes Vitamina D" (2015).

estimated that 49% of the population is overweight and 14.8% is obese according to studies from the Health Department.[49]

Dyslipidemia is often associated with obesity. According to the 2013 National Health Survey (PNS), 12.5% of the Brazilian population aged 18 and over (18.4 million people) present dyslipidemia.[50] Dyslipidemia patients are instructed to not eat foods that are good vitamin D sources, including egg yolk, liver, butter, and milk, since they present a high fat content.[51]

Therefore, the higher obesity rates in the Brazilian population are potentially related to the increase in perceived hypovitaminosis D. There are no further studies on this relationship, especially in Brazil.

Does pollution in large Brazilian centers affect vitamin D synthesis?

There are no relevant studies associating air pollution levels to hypovitaminosis D. However, it is known that air-borne impurities can absorb part of the UVB radiation, decreasing the amount reaching Earth's surface. Thus, more polluted areas may have less UVB radiation, contribution to a reduction in vitamin D levels.[33,52,53]

Studies from India and France debate the relationship between vitamin D deficiency and air pollution. A study carried out with French mothers demonstrated a potential correlation between low levels of 25 (OH) D at birth and the mother's exposure to air pollution during pregnancy.[52] The Indian study (evaluating vitamin D status in babies and children living in similar house conditions, but in two city areas with different air pollution levels) revealed significantly lower levels of vitamin D in subjects from the polluted area in comparison to those from the less polluted area.[54]

It is also questioned whether, in contrast, subjects from rural areas would have higher vitamin D levels compared to city dwellers.

Are vitamin D reference values correct for the Brazilian population?

There is a worldwide consensus that serum calcidiol levels below 25 to 30 nmol/L can damage bone metabolism.[1,55] Within this context, it is worth highlighting a discussion regarding these values, which change according to location and source, as shown in ►**Table 1**.

Currently, most services use the values suggested by the US Endocrine Society. However, their determination was based on a population sample, whose characteristics may not be representative of a given country's population.

As such, it is possible that the adopted reference levels are not suitable for the Brazilian population due to its sociocultural and environmental peculiarities.[55,56] Further studies are required to assess normal serum levels of vitamin D considering Brazilian particularities.

May values change according to sample collection, habits, and characteristics of a country's population?

According to the habits and behavior of the Brazilian population, sunscreen use may be associated with lowest 25 (OH) vitamin D levels in comparison with sunlight-exposed subjects.[21]

In addition, genetic features play a role, since it is known that the phosphate-regulating gene with homologies to endopeptidases on the X chromosome (PEX) alters the function of one of the proteins acting on phosphate regulation, which is closely linked to the diagnosis of rickets due to hypovitaminosis D.[57]

Therefore, it is essential to consider behaviors and even clinical issues from each patient to determine whether there is a diagnosis of vitamin deficiency or if these are only factors inducing the condition.

Conclusion

In a country with high UVB levels, such as Brazil, it is curious to talk about vitamin D deficiency, since UVB is the main source for the synthesis of the popular "sunshine vitamin". A few minutes under the Brazilian sun would be enough to obtain the required UVB dose for daily vitamin D synthesis.

However, a large portion of the Brazilian population presents vitamin D deficiency, although there are no populational studies quantifying it. Therefore, its potential causes are questioned.

The hypotheses raised and explored in this review indicate that reduced vitamin D levels do not result from a single factor, but a combination of sociocultural, environmental, and physiological factors, along with divergences regarding the adopted reference values.

However, there are no specific studies on the Brazilian population to elucidate the real causes of vitamin D deficiency. The questions addressed here have no definitive answers, but they would be good starting points for new inquiries.

Conflict of Interests
The authors have no conflict of interests to declare.

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