# Vitamin D Deficiency Status in Malaysia

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Vitamin D is essential for maintaining serum calcium levels, ensuring sufficient bone mineralization, immunomodulatory properties, and a protective effect on the cardiovascular system, renal disease, cancer, as well as in pregnancy. Vitamin D deficiency can be managed with pharmacological or non-pharmacological approaches, depending on the severity. The objective is to raise serum vitamin D to a normal level, hence, relieving the symptoms and reducing the adverse health outcomes. Despite no clear guidelines in treating vitamin D deficiency in Malaysia, this condition can be prevented with taking adequate vitamin D in food resources, sun exposure, or supplementation. Special attention should be given to high-risk groups including infants, obese patients, and the elderly.

Keywords: vitamin D deficiency ; prevalence ; Malaysia

### 1. Introduction

Calciferol, generally known as vitamin D, is a fat-soluble vitamin. The human body may synthesize vitamin D with the help of sunlight, specifically ultraviolet light that falls onto the skin from a precursor of cholesterol; hence, it is a non-essential nutrient [1].

Vitamin D from sunlight, food, and supplements is in an inert form; hence, it needs a biotransformation in a specific organ for activation <sup>[1]</sup>. Vitamin D is mostly synthesized endogenously when skin is exposed to ultraviolet B from sunlight which produces cholecalciferol and later is delivered to the liver by the vitamin D binding protein (VDBP). With the help of 25 hydroxylase enzymes, vitamin D undergoes hydroxylation in the liver to become 25-hydroxyvitamin D3, which is the inactive form of vitamin D. Again, the vitamin D binding protein binds to 25-hydroxyvitamin D3 and transports it to the kidney for a second hydroxylation. This activation process is carried out by the 1- $\alpha$  25 hydroxylase enzyme in the kidney that forms 1,25 dihyroxyvitamin D (1,25D). Some studies also highlighted that 1,25D can be synthesized via autocrine and paracrine action by other body tissues <sup>[2]</sup>; 1,25D is the active form of vitamin D which will act on the target organ site via diffusion or an endocytic receptor for transcription <sup>[3][4]</sup>.

Apart from sunlight, humans may also obtain vitamin D from food sources <sup>[5]</sup>. There are three types of sources which may increase vitamin D levels in human; they are natural foods, fortified food, as well as supplements. Vitamin D is mostly found in fatty fish such as salmon, mackerel, herring, tuna, and sardines, but it is also abundant in cod liver oil and egg yolk <sup>[1][6]</sup>. Meanwhile, vegetables, meat, and poultry are poor sources of vitamin D. For fortified food, it can be found mainly in cereals, bread, butter, yogurt, and milk, and they are mostly on a volunteer basis by the manufacturer. For supplements, vitamin D is usually combined with calcium or with a multivitamin formulation <sup>[1]</sup>.

### 2. Epidemiology of Vitamin D Deficiency

The 25-hydroxyvitamin D (25(OH)D) level is utilized to reflect dietary and endogenously acquired vitamin D. With a long half-life of 15 days, 25(OH)D can be found in plentiful concentrations in the body [5]. However, the accuracy of the diagnostic test and its standard references are not clearly stated and are varied according to different studies [5][ $\mathcal{I}$ ]. Despite the differences in the value of deficiencies, the published cut-off value is usually 30 nmol/L and often falls within the range of 25 to 30 nmol/L. The definition for insufficiency is serum 25(OH)D between 30 to 50 nmol/L [9][ $\mathcal{I}$ ].

#### 2.1. Adults

A multi-ethnic study involving male and female teachers in Kuala Lumpur, Malaysia showed that 67.4% has vitamin D deficiency (<20 ng/mL), which was comprised of Indian (80.9%), Malay (75.6%), others (44.9%), and Chinese (25.1%) <sup>[10]</sup>. According to a study among Malay men and women, 87% of women suffered vitamin D deficiency compared to 41% of men <sup>[11]</sup>.

#### 2.2. Menopausal Women

Studies showed that women's vitamin D levels are lower on average, and because of this, special populations such as menopausal women need to be highlighted. A study among Chinese postmenopausal women (menopause period more than 5 years) in two main urban cities of Malaysia revealed that the majority had serum vitamin D deficiency (82.7%) <sup>[12]</sup>. Meanwhile, a multi-ethnic (Malay and Chinese) study on postmenopausal women aged 50 to 65 years in Kuala Lumpur discovered that 26.7% of Malay and 87.8% of Chinese women had vitamin D hypovitaminosis. Furthermore, there was a substantially higher prevalence of deficiency among Malay postmenopausal women when compared to Chinese women, which were 71.3% and 12.2% respectively. It was shown that the level of 25 (OH) D among Malay women was 44.4 nmol/L, whilst the Chinese recorded a level of 68.8 nmol/L  $^{[13]}$ .

#### 2.3. Pregnant Women

According to the World Health Organization, in certain populations around the world, vitamin D deficiency is considered a frequent occurrence among pregnant women, and it has been linked to an increased risk of pre-eclampsia, gestational diabetes mellitus, premature delivery, and other tissue-specific disorders. A study that enrolled first trimester women 18 to 40 years old in Selangor reported that hypovitaminosis D was 90.4 percent <sup>[14]</sup>. On the other hand, a total of 50.2% of women in their third trimester (37 weeks and above) were vitamin D deficient <sup>[15]</sup> compared to 42.6% among those who were pregnant at 28 weeks <sup>[16]</sup>.

#### 2.4. Adolescents

A large study involving 1361 adolescents aged 12 to 13 years old in Perak, Selangor, and Kuala Lumpur revealed that 78.9% had vitamin D deficiency; 1.5% were severely deficient; and 13.7% were having insufficiency. Only 7.4% of the individuals had an adequate level of vitamin D  $^{[17]}$ . The same study showed that the serum vitamin D mean level for males was 37.4 nmol/L (±1.2) and for females was 24.2 nmol/L (±0.6), with the Indians having the lowest mean value. Another study in Kuala Lumpur and Selangor comprising of 1061 15-year-old adolescents found that vitamin D deficiency was 33%  $^{[18]}$ .

#### 2.5. Children

The South East Asian Nutrition Survey (SEANUTS) was conducted throughout Malaysia from 2010 to 2011 (Sabah, Sarawak, and Peninsular Malaysia), encompassing 3542 children aged four to twelve years old. Blood parameters revealed that 47.5% had low vitamin D levels, with girls (54.1%) having a substantially greater prevalence than boys (41.1%) <sup>[19]</sup>.

# 3. Statistics of Global Vitamin D Status

Recent statistics of global vitamin D status around the world revealed that vitamin D deficiency and insufficiency are ubiquitous regardless of the latitude of the countries, and, even in high income countries, vitamin D deficiency persists despite their capabilities of fortification efforts aimed at assuring adequate intake <sup>[20]</sup>. Unfortunately, to pinpoint the most vulnerable groups exactly in terms of geographical location or countries is quite difficult due to the lack of standardized data in many countries. The available data are derived mostly from out-of-date studies (ten years and above), and the majority involved small studies rather than large surveys. Nevertheless, evidence indicates that vitamin D deficiency is more prevalent in Africa, the Middle East, and Asia <sup>[Z][21]</sup> with an inclination towards female gender, particularly in pregnant and lactating women, the elderly, and those involving the use of extensive coverage of the skin, thus limiting exposure to sunlight. Additionally, there are substantial data gaps, particularly for lower middle-income countries and those pertaining to obesity which can also contribute to the problem in this current era.

It showed that through all the ages, with or without underlying disease, female gender tends to have a lower mean level of serum 25(OH)D concentration and a higher prevalence of vitamin D deficiency. High prevalence of low vitamin D levels may be related to several issues. It is known that vitamin D is mostly obtained from sunlight <sup>[22][23]</sup>. The synthesis of vitamin D3 under the skin is affected when the transmission of solar UVB radiation to the earth's surface or UVB radiation penetration into the skin is affected <sup>[24][25]</sup>. In this context, skin type is an important factor in which melanin is very effective at absorbing UVB rays and shields the skin underneath. However, vitamin D production in the skin is further hampered by the reduced amount of UVR that is accessible <sup>[26]</sup>. Dark skin is known to have a low capacity to produce vitamin D <sup>[27][20]</sup>. This is consistent with the studies reported in Malaysia whereby the darker skin ethnicities (Indian and Malay) have a lower vitamin D mean level and are more susceptible to vitamin D deficiency and insufficiency <sup>[17][9][10][14][13]</sup>.

Sun avoidant lifestyles such as the use of sunscreen, conservative clothing habits, and outdoor inactivity are also some of the important causes of low vitamin D status. A sunscreen applied topically absorbs incoming UVB light, thus reducing vitamin D3 production in the skin <sup>[28]</sup>. Type of dress which involved covering the entire skin and preventing it from being exposed to sunlight also prevents the absorption, which explains why vitamin D deficiency is so widespread even in the sunniest parts of the world <sup>[15][29][30][31]</sup>. This can be seen in populations where extensive skin coverage was practiced by the women as part of their religion or cultural norm, which is often described in studies in the Middle East, and Central and South America. A study in Malaysia among multi-ethnic pregnant women in their third trimester found that veiled clothing was significantly associated with vitamin D deficiency <sup>[15]</sup>. Furthermore, individuals who are confined to their homes or work in jobs that limit their exposure to sunshine are unlikely to receive enough vitamin D from sunlight <sup>[32]</sup>.

Human milk alone is not able to provide the vitamin D requirement for infants <sup>[33]</sup> unless pregnant mothers are supplemented with a high amount of vitamin D <sup>[34]</sup>. Thus, breastfed infants are among the vulnerable groups who are at risk to have a low vitamin D status. Nevertheless, a lot of other factors need to be considered since mothers are not routinely given vitamin D supplements; exclusively and partly breastfed babies should be considered to be given 400 IU of vitamin D per day <sup>[34]</sup>, which is the recommended daily requirement throughout infancy (American Association of Pediatricians (AAP)).

A reduced amount of the precursor (7-dehydrocholesterol) of vitamin D3 in the skin is also linked to aging <sup>[35]</sup> in which the skin of the elderly is unable to manufacture vitamin D as effectively as in the younger people. Other factors that made them more prone to have a low level of vitamin D are increased indoor time due to their limitations <sup>[33]</sup>.

An obese person has lower serum 25(OH)D levels. They require higher vitamin D doses than normal to attain the levels equivalent to those of healthy weight individuals <sup>[33]</sup>. Since vitamin D is a fat-soluble vitamin, it is easily absorbed by fat cells; thus, there will be less of it in the circulation. For those with gastric bypass surgery, the portion of the upper small intestine where vitamin D is absorbed is skipped; thus, without enough vitamin D from the diet or supplements, this group of people is more susceptible <sup>[36][37]</sup>.

Among the consequences of vitamin D deficiency are nutritional rickets which can be attributed to the lack of vitamin D or dietary calcium or both even in the absence of overt deficiency <sup>[38]</sup>. Bone mineralization is sustained by an interaction of vitamin D and calcium. When there is appropriate calcium intake, 25(OH)D more than 30 nmol/L is sufficient to avoid nutritional rickets <sup>[39]</sup>. Severe vitamin D deficiency can cause a decreased level of calcium, phosphate, or phosphorus, leading to improper mineralization of the bone. These in turn can give rise to osteomalacia in adults <sup>[40]</sup>. Babies are at risk of congenital rickets and hypocalcemia if their mothers have vitamin D deficiency <sup>[41][42]</sup>. Other than preventing congenital rickets and hypocalcemia, pregnant mothers supplemented with vitamin D will be less susceptible to pre-eclampsia, having low birth weight newborn, and preterm delivery <sup>[8]</sup>.

Vitamin D deficiency can be managed with pharmacological or non-pharmacological approaches depending on the severity. The goal of the treatment is to raise serum vitamin D to normal levels to relieve the symptoms and reduce the adverse health outcomes such as rickettsia among infants, osteomalacia among adults, and osteoporosis among the elderly. To date, there are no clear guidelines in treating vitamin D deficiency in Malaysia.

Vitamin D can also be acquired from natural food sources such as eggs, meat, fish (mackerel, salmon, sardines), and fish oils. The best source of vitamin D comes from animal products. Vegetarians can obtain dietary vitamin D from mushrooms or other fortified products such as dairy products, bread, orange juices, and cereals <sup>[1][43]</sup>.

# 4. Conclusions

Even though Malaysia is a tropical country, the population still suffers from vitamin D deficiency and insufficiency, a finding which is consistent with research from other countries. It is imperative to investigate further the causes of the high prevalence of low vitamin D levels with standardized guidelines for the vitamin D level definition, larger sample sizes, and solid methodologies. The latest evidence showed that vitamin D is important for the prevention of multiple non-communicable diseases, and it has significant roles in other organ functions. Especially during this COVID-19 pandemic, whereby the presence of underlying inflammation determined the severity of COVID-19 illness, and low levels of vitamin D are associated with a significantly increased risk of pneumonia and viral upper respiratory infections. With these in mind, there should be more effort and investment put into the empirical research to be incorporated into effective interventions to reduce the burden of vitamin D deficiency and thus other preventable diseases. Regulatory bodies should make vitamin D content in Malaysian food composition table as mandatory. In addition, the vitamin D fortification in Malaysia should be regulated and standardized to control this issue.

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