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Review

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Prevalence of vitamin D deficiency in Libya and its relation to other health disorders

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Abstract

Vitamin D (VD) has a potential role in calcium homeostasis in the human body. It is also considered a strong immunomodulator, affecting both arms of the immune system (Innate and adaptive immunity). VD can also lower the risk of diabetes, improve pregnancy outcomes, reduce the risk of acute respiratory infection (e.g., COVID-19), and decrease the risk of cancer. No doubt that VD deficiency (VDD) is a health condition that spreads out all over the globe. VDD is linked to many health problems ranging from fatigue and skeleton pain to serious conditions such as rickets, osteomalacia, diabetes, autoimmune disease, cardiovascular diseases, and cancer. This review aims to provide a whole picture of the status of 25- hydroxycholecalciferol [25-(OH)D] as well as the frequency of 25-(OH)D deficiency (VDD) among Libyans in various regions of the country and to discuss the correlation between VDD and other health problems. The prevalence of VDD reached up to 80% among healthy individuals in the Middle East region. Libya is a big Mediterranean country and is sunny most of the year. In the western part of Libya, particularly in Tripoli (the capital city), the prevalence of severe VDD [25-(OH)D < 10 ng/mL] was as high as 50.8%, whereas only 27.5% had moderate VDD [25-(OH)D; 10-20 ng/mL]. In Benghazi (second largest city), the VDD prevalence was also high (76%). The highest prevalence of VDD was reported at 79% in the biggest southern city of Sebha. In the whole country, the VDD prevalence was high (among males and females), ranging from 45.4% to 87%, with a mean of 55.58%. The mean prevalence of VDD among males was 54.3% and for females was 53.29%. As clear from these data, VDD prevalence was high in the entire country. However, the available data were obtained from small cross-sectional studies and it becomes a necessity to conduct nationally representative studies and establish national nutrition surveys to accurately assess the prevalence of VDD. Moreover, the data included in this review invites the health authorities in Libya to take preventive measures to reduce the high

prevalence of VDD, which will decrease VDD-associated health problems in the future.

Keywords: 25- hydroxycholecalciferol, Vitamin D deficiency prevalence, rickets, osteomalacia

INTRODUCTION TO SYNTHESIS AND PHYSIOLOGICAL ROLES OF VITAMIN D

Vitamin D (VD) is a fat-soluble vitamin originating from cholesterol under the skin via exposure to sunlight; hence, it is called the sunshine vitamin. Mellanby was the first scientist to discover VD in 1,920 in ng/mL[1]. About 80% of VD is synthesized beneath the skin by the direct penetration of sun radiation (specifically, UV radiation B with a wavelength of 290-320 nm), which alters 7-dehydrocholesterol to previtamin D3. Only 20% of the daily requirement of the vitamin was provided by the diet or VD supplements[2]. The dietary sources of VD include fatty fish such as mackerel and salmon, and VD-fortified foods such as milk and cereals. VD supplementation usually contains vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol). However, VD3 is more effective in increasing and maintaining the serum levels of VD[3].

The active form of VD is 1,25- hydroxycholecalciferol [D3; 1,25(OH)2D], which is formed by the hydroxylation of the inactive or the storage form 25- hydroxycholecalciferol [25-(OH)D] in the kidneys. Research evidence suggested that the ectopic production of 25-(OH)D-(3)-1α-hydroxylase 1 (α-OHase) has been recognized for a long period. The mitochondrial cytochrome P450 enzyme 25-OH VD3-1α-hydroxylase is the rate-limiting enzyme in the process of hydroxylation of 25-(OH)D to produce the active form 1,25-(OH)D[4,5].

Studies showed that the physiological actions of VD were performed by altering the gene expression through direct effect on nuclear DNA; this mode of action is similar to that of steroid hormones[6,7].

No doubt that VD deficiency (VDD) is a health condition that spreads out in the whole world. VDD becomes a pandemic affecting about one billion individuals around the globe and the condition is not restricted to specific ethnical backgrounds or geographical locations. VDD is detected by the measurement of the serum concentration of 25-(OH)D. VDD affects both genders (males and females) of all age groups. Furthermore, VDD is linked to many health problems, including rickets in children and osteomalacia in adults. Beyond these classical disorders, VDD is also believed to have a role in the development of many conditions ranging from fatigue and skeletal pain to serious disorders including diabetes, cardiovascular diseases (CVDs), and cancer[8]. Researchers found that increasing 25-(OH)D levels in many inflammatory and chronic diseases, such as CVDs, type 2 diabetes (T2DM), Alzheimer's disease, and cancer, have ultimately led to a reduction in the mortality rate by 11% in the Middle East area and an increase in the life expectancy by 2 years[9-11]. Table 1 contains a summary of the most important functions of VD in the human body.

The sunlight exposure to achieve optimum photosynthesis of VD under the skin is affected by numerous factors, including season, country or city geographical location, and personal characteristics (e.g., skin type). Regarding the location, the distant areas located north or south of the equator significantly influence the intensity of sun and UVB radiation. Areas located closer to the equator receive more intensive sun rays during the whole year. Consequently, individuals living in equatorial locations have more chances for adequate VD production. On the other hand, locations at higher latitudes are exposed to diminished UVB radiations, especially during the winter season. Consequently, this leads to decreased exposure, which in turn restricts the ability of the skin to synthesize VD[18]. The climate and seasonal changes can influence VD

Table 1. Summary of the important functions of VD

Function	Physiological role of VD
Calcium homeostasis	VD stimulates dietary calcium Ca^{+2} absorption in the small intestine to maintain Ca^{+2} in the blood. Ca^{+2}, in turn, is essential for bone health, muscle contraction, and nerve signalin[12]
Bone health	VD aids in bone mineralization, where it helps strengthen the bone matrix by the incorporation of Ca^{+2} and phosphorus. Lack of VD leads to enhanced risk of bone fractures and osteoporosis[13]
Modulation of the immune system	As an immunomodulator, VD influences both innate and adaptive immunity. VD stimulates the synthesis of antimicrobial proteins such as cathelicidins and defensins. VD also regulates the proliferation and differentiation of T and B cells[14]
Cell growth and differentiation	VD has a vital role in differentiating many cell types in various tissues, including skin, prostate, breast, and colon. It also maintains proper growth and differentiation Moreover, VD prevents abnormal cell proliferation, which is always linked to tumors[15]
Cardiovascular health	VD is believed to affect the regulation of blood pressure and endothelial function. Research linked VDD to enhanced risk of hypertension, heart disease, and stroke. The mechanism by which VD influences cardiovascular health still needs further research[16]
Mental health	The Potential role of VD in mental health is indicated by the presence of VD receptors in the brain tissues. VDD has been associated with disorders of mood (e.g., depression and seasonal affective disorder (SAD)[17]

production. Adequate VD synthesis is usually achieved in the summer season, during which the sunny climate allows direct and continuous exposure to sunlight. However, in the winter, the sun's position is low in the sky, leading to diminished UVB intensity and limited exposure durations[19]. Health professionals have suggested several approaches and recommendations to enable individuals to promote the optimum synthesis of serum 25(OH)D (a marker of vitamin D status in humans) [Table 2].

Libya is one of the largest and richest countries on the Mediterranean Sea's southern coast. Due to climate change and the continuous rise of the ambient temperature, coupled with the modern lifestyle forcing many people to work from home using the internet, exposure to sunlight has been extensively reduced. Furthermore, a large percentage of the Libyan population adapted to a sedentary mode of office work, especially in the urban cities. Furthermore, a large proportion of the Libyan population are young people and the vast majority of them are students who are influenced by modernization and sedentary lifestyle, making them more prone to develop VD deficiency symptoms primarily due to decreased exposure to sun radiation, which is essential for the internal synthesis of VD through the process of photosynthesis[24]. The following includes an evaluation of VD status among the Libyan population in many Libyan cities in different parts of the country.

VITAMIN D DEFICIENCY STATUS IN DIFFERENT LIBYAN CITIES

Method

The measurement of serum VD in the different studies included in this review was done using the ELISA Method for the quantitative determination of serum of 25-(OH)D. The electrochemiluminescence protein binding assay (ECLIA) to investigate serum 25(OH)D by Roche Diagnostics, Cobas e411 analyzer, was used to measure the serum levels of 25-OH VD in most of the studies conducted in the various Libyan cities included in this review[25]. The technique has a sensitivity of 3 ng/mL for 25-OH vitamins D2 and D3. Anti-25-OH vitamin D3 antibodies detect the presence of 25-OH VD indicated by peroxidase activity and measured as a substrate OD at 450 nm. Results are expressed as ng/mL. The included studies represent various geographical areas of the country. All the stages of data analysis were accomplished based on the concentration range of serum 25-(OH)D as shown in Table 3[26]. To have an overall image describing the prevalence of VD deficiency using serum 25-(OH)D concentration among all the populations included in the various studies, we calculated the average percentage of the sum of all the prevalence values obtained from the studies conducted in the different Libyan cities.

Table 2. Includes recommendations for getting adequate VD by photosynthesis

Recommendations	Details
Exposure duration and timing	Health professionals advised individuals to be exposed to sunlight for 10 to 30 min during midday (10 a.m. to 3 p.m.) at least 2 to 3 times/week. The exposed body areas are the face, arms, legs, or back[20]
Exposure without Sunscreen or Protective Clothing	Sunscreen blocks UVB radiation, so its use during sun exposure should be avoided. However, it is important to balance between getting adequate VD and protecting the skin from UV radiation. Short periods of exposure are highly advised for UV-sensitive people who have a family history of skin cancer[21]
Instructions for Individual variation:	Exposure time should be designed according to individual factors (e.g., skin type and geographical region). People with darker skin require longer exposure than those with lighter skin for adequate VD synthesis. People living at higher latitudes, especially in winter, may require longer duration to overcome low UVB intensity[22]
Adjustments for Health conditions	People with specific health disorders or on drugs that influence the metabolism of VD should consult their doctors to detect adequate sunlight exposure periods. Moreover, persons who have a high risk of developing skin cancer should seek other sources of VD, e.g., VD supplementation[23]

Table 3. The reference levels used in the analysis of 25-(OH) D in human serum

VD status	Range (ng/mL)
Poor (Severe Deficiency)	5-9.9
Deficiency	10.1-19.9
Insufficiency	20.1-30
Adequacy	30-80

An overview

Recent studies suggested that the prevalence of VDD and rickets was higher in the Middle Eastern populations compared to their counterparts' Western populations. It was estimated that the prevalence of VDD was 20%-80% among healthy subjects in Middle Eastern countries; this finding was presented in a large meta-analysis study[27]. This review is the first to our knowledge that collected data from many studies that investigated VD status in a wide variety of Libyan regions located in the main provinces of the country. The results showed a high total prevalence (54.3%) of 25-(OH)D deficiency in the different Libyan cities included in this review. Table 4 summarizes the prevalence of VDD and mean ± SD of serum levels of 25-(OH)D. However, this work had some limitations; firstly, the studies included in this work evaluated the serum levels of 25-(OH)D but were conducted in different years and different climate seasons, although the difference in climate seasons has a low effect on 25-(OH)D levels because Libya has sunny weather all the times of the year. Secondly, the data included in these studies were obtained from both genders, but the results showed the levels of 25-(OH)D for males and females separately. Finally, the data of 25-(OH)D were derived from small cross-sectional studies, which invite us to point out the need to conduct large nationally representative studies in combination with a national nutrition survey of VD status in various regions of Libya.

The VD status was interpreted according to cut-off values reported by the Institute of Medicine (IOM) in 2011[37], but there is a need to unify and generalize these cut-off levels of 25(OH)D in the whole country. Future studies for evaluating serum 25(OH)D should also follow the assay standardization of serum 25(OH)D measurements. A standardized measurement is accurate and comparable over time, location, laboratory procedure, or assay. The international Vitamin D Standardization Program (VDSP) has developed and published various statistical approaches for standardizing the measurement of serum 25(OH)D concentration. Moreover, standardization implies that each laboratory reports the same results for the same samples. It not only assures that the assessment of prevalence at any one time is correct, but also it assures that monitoring over time permits the identification of the differences in prevalence over time. The international Vitamin D Standardization Program (VDSP) has developed and published various statistical approaches for standardizing the measurement of serum 25(OH)D concentration[38]. The

Table 4. Prevalence of VD deficiency detected by measuring the serum levels 25-(OH) D in various Libyan cities

Libyan city	Age range (years)	VDD	
		mean ± SD ng/mL	%
Tripoli[28]	18-65	M: 16.6 ± 9.8 F: 13.6 ± 11.3	M+F: 45.42%
Tripoli[29]	20-50	M: 13.9 ± 3.5 F: 11.3 ± 4.2	M: 25.58% F: 79.26%
Tripoli[30]	18 80	F: 14.2 ± 0.3	F: 27.4%
Alejelat[31]	1-80 47% (21-40)	NA	M: 57.45% F: 69.5%
Benghazi[32]	18-80 M = 36.2 ± 0.9	M+F: 13.9 ± 0.7	M+F: 76%
Sirte[33]	26-65	M+F: 13.2 ± 3.7	M+F: 48.8%
Tobruk[34]	1-40 > 40	M: 22.3 ± 0.8 F: 20.5 ± 0.5	52.1%
Sebha[35]	18-25	M+F: 12.3 ± 5.0	M+F: 79%
Wadi Etba[36]	20-40	F: 14.7 ± 2.8	F: 37%

NA: not available; M: males; F: females; m: mean; SD: standard deviation.

following parts of this review describe the results of serum 25-(OH)D concentrations in the populations of the major cities distributed in various geographical areas of the country to give a generalized evaluation of VD in this large country.

VD status in the capital city of Tripoli

Tripoli is the largest and most populous city in the country. It is located on the western coast of Libya, facing the Mediterranean Sea, and it has sunny weather almost during the four seasons of the year. In a very recent cross-sectional study, Aljazzaf and others investigated the correlation between VD and the health condition of 306 subjects in the period between April 2019 and March 2020. The subjects were of both genders and they were further divided according to age into young adults (18-25 years) and adults (26-65 years). Study subjects attended various hospitals and clinics, such as Tripoli University Hospital, which provides health services to the vast majority of the population in Western Libya, including the capital, Tripoli. Serum 25-(OH)D was measured by electrochemiluminescence protein binding assay (ECLIA) using Roche Diagnostics, Cobas e411 analyzer.

The study found that about 90% of subjects had serum 25-(OH)D values less than the normal range (< 30 ng/mL), whereas 45% of them were severely deficient in VD [serum 25-(OH)D levels were <10 ng/mL] and 44% were 25-(OH)D insufficient (20-29.9 ng/mL). The authors concluded that the higher prevalence of VD deficiency harmed the health status. Adult females with VD deficiency were at a higher risk of sleeping problems, psychological manifestations, headache, and osteoporosis, whereas their male counterparts had an increased risk of developing obesity and diabetes mellitus (DM)[28]. Serum 25-(OH)D levels were investigated by direct ELISA kit method using vitamin D ELISA Kit (ORGENTEC Diagnostika GmbH Company - Germany).

A very recent work by Ahmed *et al.* in 2023 aimed to assess the prevalence of 25-(OH) D deficiency among 293 adult individuals (129 males and 164 females; their age range was 20-50 years) in the Tripoli region. The study also aimed to evaluate the contributing factors for VDD, including age, gender, and obesity. The total prevalence of VDD was 55.63% (out of which 25.58% were males and 79.26% were females). The prevalence of 25-(OH)D insufficiency (20-30 ng/mL) was 19.45% of the study subjects (23.25% males and 16.46%females). Furthermore, 24.91% of the subjects had normal 25-(OH) D (51.16% males and 4.26%

females). The highest prevalence of VDD was among subjects of the age group 41-50 years. The mean level of 25-(OH)D of males (13.93 ± 3.46 ng/mL) was significantly higher compared to that of females (11.32 ± 4.16 ng/mL). The authors concluded that obesity appeared to have unfavorable effects on 25-(OH) D values, which may lead to severe VDD[29].

In a cross-sectional study in Tripoli, Al-Graiw *et al.* investigated 25-(OH)D status in 262 female subjects (age range; 18-80 years) suffering from nonspecific musculoskeletal and bone pain during the period from January 2017 until December 2017. Serum 25-(OH)D was measured using an ELISA kit provided by Roche Diagnostics Co., Ltd., Germany, following the American Society for Testing and Materials communication protocol (ASTM communication protocol) on Cobas 411 Automatic Electrochemiluminescence Immunoassay Analyzer (Roche Diagnostics, Mannheim, Germany). The mean level ± standard deviation of 25-(OH)D of the whole study participants was 13.98 ± 10.2 ng/mL. 51% of the total cases showed severe VDD [25-(OH)D levels < 10 ng/mL], whereas the prevalence of moderate VD deficiency was 27.5% [25-(OH) D levels 10-20 ng/mL], and only 9% of subjects had insufficient VD. Out of the total number of subjects, only 13% showed sufficient levels of 25-(OH)D (≥ 30 ng/mL). Furthermore, subjects who consumed low amounts of fish and milk showed a mean 25-(OH)D level of 8.1 ± 0.9 ng/mL, which was significantly ($P < 0.000$) lower compared with subjects who consumed higher amounts of fish and milk (23.3 ± 0.17 ng/mL). The author of the study concluded that the conditions of non-specific body aches, fatigue, and bone pains were significantly correlated to VD deficiency status[30].

VD status in Alejelat city in the Western region of Libya

An observational study in 2019 investigated VD status in 377 individuals (141 males and 236 females, their ages ranged from one to 80 years) for 6 months from the first of March 2019 to the 30th of August 2019. Exclusion criteria included the use of any treatment known to influence bone metabolism, such as seizure drugs phenobarbital, anti-tuberculosis drugs, cholesterol-lowering statin drugs, thiazide diuretics, antiretroviral drugs, and glucocorticoids. Serum 25-(OH)D was investigated using an enzyme immunoassay method. The Overall prevalence of severe VDD [25-(OH)D < 10 ng/mL] was 39.26%, moderate VDD [25-(OH)D 10-20 ng/mL] was 25.73%, VD insufficiency [25-(OH)D 21-29 ng/mL] was 17.8%, whereas adequate VD levels [25-(OH)D ≥ 30 ng/mL] represented only 17.24% of the total study population. The study subjects were further divided into different age groups (in years): (1-20), (21-40), (41-60), and (61-80). The prevalence of severe VDD was 5%, 10.1%, 8%, and 3.7%, respectively, and the prevalence of moderate VDD (11-20 ng/mL) was 4.8%, 23.6%, 4%, and 4.2%, respectively. These results showed that the majority of VD-deficient cases were among the young adult age group (21-40 years). Moreover, this study found that VD deficiency was greater in females (69.49%) than in male subjects (57.45%)[31].

VD Status in the largest Eastern Libyan city "Benghazi"

Libya is one of the large Middle Eastern countries located on the southern coast of the Mediterranean Sea. Benghazi is the second largest city situated on the eastern coast of Libya, where people enjoy the sunshine all over the year. Although the exposure to the sun is adequate, higher rates of VDD were reported in sunny climate regions[39,40].

In a cross-sectional study in the Benghazi area, 184 subjects were purposefully recruited from three polyclinics in Benghazi between July 1st and September 30th, 2016. The age range of the participants was 18-80 years, with a mean age of 36 ± 1 years for females and 37 ± 4 years for males. Subjects were excluded if they were taking any drugs that affect bone metabolism, and previously VDD-diagnosed and receiving VD supplements at the time of study. ELISA, an enzyme-linked immunosorbent assay, was the test used to investigate 25(OH)D in the serum of the participants[41].

The prevalence rate of vitamin D deficiency was 76.1%, whereas 15.2% showed VD insufficiency (21-29 ng/mL) and interestingly, only 8.7% of the study population showed normal 25-(OH)D levels. This study also predicted that the behavior style of avoiding exposure to the sun to get a lighter skin appearance was the major contributing factor to high VDD rates among both genders in the study[32]. This work was in agreement with a study in Saudi Arabia, which found that the VDD subjects tended to prevent skin darkening by avoiding direct exposure to the sun, which, in turn, reduced the internal synthesis of the vitamin[33]

VD status in Sirte (the central coastal city of Libya)

In the last quarter of 2022, a study was conducted in the main city of the central coast of Libya, which aimed to evaluate 25-(OH)D deficiency and its relation to the age and sex of 244 individuals (28.7% males and 71.3% females) attending five medical laboratories. The study found that 119 subjects had experienced different categories of VDD (48.8%), and the majority of them (59.66%) belonged to the 26-65 years age group. The mean serum level of 25-(OH)D was 13.23 ± 3.7 ng/mL. 21.7% of the study population experienced severe VDD [25-(OH)D was less than 10 ng/mL]. The authors also reported that females appeared more prone to VD deficiency compared to males[42]. Furthermore, in the subjects into age groups, the greatest VDD prevalence was within the 25-65 years group (59.66%) followed by the 11-25 years group (28.6%), whereas a prevalence of 9.24% was reported for subjects older than 65 years.

Vitamin D status in the city of Tobruk

The city is the farthest on the eastern Libyan coast on the Mediterranean Sea (about 100 Km from the country's borders with Egypt). The climate is identical to that of Benghazi with the sun shining most of the year which enables people to be adequately exposed to the sun many times during the week to get their needs of the VD internal production.

A recent study performed by Bougafa and Tahir included 568 subjects (169 males and 399 females) attending the Ibn Rashid Laboratory in Tobruk city. The serum 25-(OH)D levels were measured by the previously mentioned ECLIA assay by Cobas machine e 411. The prevalence of VDD was the greatest with 296 subjects (52.1%). Moreover, the highest frequency of VDD was observed in females (n = 255) with 56.4% compared to 42% among male subjects (n = 71). The overall mean 25-(OH) D levels of male participants (n = 169) 22.30 ± 0.80 ng/mL were significantly (P < 0.05) higher than that of females (n = 399) 20.48 ± 0.48 ng/mL[34]. These results were in agreement with the work of Agila, 2020 who found that 57.4% of the subjects experienced VDD in the same city "Tobruk". The author showed that 61.8% of the participants were mostly not exposed to sunlight and did not include VD-rich food or supplements in their diet[43]. It is important to mention that VD dietary sources and VD supplements become significantly important sources of the vitamin, particularly in the areas deprived of sunlight radiation.

VD status in Sebha City and Wadi Etba Area in Southern Libya

Recently, Alaasswad *et al.* investigated VD levels among 79 pharmacy students attending the University of Sebha. The blood samples were collected randomly from 79 students aged 18-25 years and tested for serum 25-(OH)D levels by ELISA test. The prevalence of VDD was very high (79%). Their mean serum level of 25-(OH)D was 12.3 ± 5 ng/mL, whereas 8.0% of students showed VD insufficiency and only 8 students (13%) had normal 25-(OH)D levels (51.9 ± 17.5 ng/mL). Furthermore, the study reported that a high incidence of VDD was accompanied by high prevalence of anemia[35].

In another novel study, our research group evaluated VD status and calcium levels among 622 females of reproductive age (20-40 years) attending the Rural Hospital and Private Clinics in Wadi Etba located in the southern region of Libya during the last five years (between January 2017 to December 2021). The study

population was further divided into two age groups: 20-30 years and 31-40 years. ELISA test was used to investigate 25(OH)D in the serum of the participants. The authors found that the vast majority of 489 subjects (78.6%) had sub-optimal serum 25-(OH)D levels (< 30 ng/mL), whereas only 133 subjects (21.4%) presented with normal serum 25-(OH)D levels values (more than 30 ng/mL). The results also showed that more than half (57%) of the study population experienced VD deficiency in 354 subjects (serum levels of 25-(OH) D; lower than 20 ng/mL). Moreover, out of the VD-deficient females, 122 subjects (20%) presented with severe VD deficiency [25-(OH)D < 10 ng/mL], and their mean serum 25-(OH)D level was 8.2 ± 0.6 ng/mL. Concerning serum calcium levels, the study reported that about a third of the total population (31%) had calcium levels lower than the normal range, whereas 68% had normal calcium levels. On the other hand, serum calcium levels were not significantly correlated with serum 25-(OH)D levels[36].

DISCUSSION

Association of VDD with various health conditions beyond bone disease

The prevalence of serious conditions of bone diseases (rickets and osteomalacia) is high even in areas with sunny climates that are supposed to enhance the synthesis of VD depending on exposure to sun radiation. In general, the worldwide prevalence rates of VDD are ranging from 30% to 90%. It has been believed that the continuity of breastfeeding without supplementing the infants with VD and reduced calcium in the diet are the major risk factors for the high prevalence of rickets and VDD in infants and children. VDD is also linked to pain score and disease activity in rheumatologic disorders[44]. Furthermore, VD is implicated in these conditions due to its potential role as an immunomodulator[45]. VD is involved in regulating both innate and adaptive immunity. VDD can disrupt the immune response, causing a defect in the body's defense against microbes, which leads to an increase in the incidence of infections[46].

Consequences of VDD on acutely and chronically ill patients

Research studies believe that the diminished role of VD as an immunomodulator has been implicated in many health problems, including osteoporosis, cardiovascular diseases, autoimmune diseases, and cancer. Furthermore, recent research revealed that VD has an anti-inflammatory role, which can help mitigate excessive inflammation. This action may be involved particularly in the states of dysregulation of inflammation, such as hyperinflammatory conditions and cytokine storms, which ultimately lead to a decrease in the risk of complications related to inflammation[47]. Table 5 includes the various influences of VDD on acute and chronic diseases. VDD may also have critically ill patients and its potential consequences extend to chronic conditions. VD deficiency is linked to a high risk of the incidence of fatigue and unexplained bone pain. No doubt that these health issues had negative effects on the performance of the workers at workplaces as well as their social activities outside of work. Roy *et al.* reported a high prevalence of VDD (77.2%) in subjects who suffered from fatigue. Interestingly, those patients improved by consumption of VD supplements to normalize their serum levels of 25-(OH)D[53].

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Table 5. Various effects of VDD on acutely and chronically ill patients

Effect of VD deficiency	Details
Immune response impairment	VD is an immunomodulator. VDD can interrupt the immune response and impair the defense process against infections, thus enhancing the risk of acquiring infections[48]
Muscle weakness	VD plays a vital role in muscle strength and function. VDD may cause weakness in muscles[49]
Enhanced risk of falls in critically ill patients	A higher risk of falls occurs due to muscle weakness resulting from VDD in critically ill cases. This risk is more obvious in hospitalized old patients who find difficulty in movement[50]
Extended patient hospitalization	VDD is linked to prolonged hospital stays, increasing the costs of healthcare. Moreover, it may contribute to enhancing the risk of incidence of complications related to long hospital stays (e.g., infections)[51]
Worsening the conditions of chronically ill patients	For instance, it can exacerbate osteoporosis by disrupting Ca^{+2} absorption, which influences bone health. It may also exacerbate the complications of cardiovascular disease, such as atherosclerosis and hypertension. It also causes worsening of the respiratory disorders, for example, chronic obstructive pulmonary disease (COPD) and asthma[52]

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Vitamin D plays a vital role in the nervous system function and VDD has been linked to mental and psychological abnormalities such as depressive symptoms and impaired cognitive performance[54]. Moreover, VD has also been linked to fatigue and other unspecific conditions including musculoskeletal pain and general weakness[55]. In a randomized controlled trial, there was an improvement in the symptoms of muscle pain by normalization of VD in patients presented with vitamin D deficiency[56]. On the other hand, there was no improvement in chronic fatigue syndrome (CFS) found following the administration of high-dose VD3[57].

Extra-renal hydroxylated VD role in the treatment of proliferative disorders

Previously, 1α-hydroxylase was believed to be a kidney enzyme, but currently, it is confirmed that it is produced in various tissues, for instance, the brain, placenta, adrenal medulla, and pancreas[58].

The role of 1α-hydroxylase in extra-renal tissues has been suggested as a protective mechanism, which is referred to as a 'barrier function' that includes antiproliferative and immunomodulatory influences via epithelial, endothelial, and immune system cells[59]. Macrophages were among the first extrarenal cells that demonstrated the capacity to produce $1,25(OH)_2D_3$. The macrophages have shown this role once they were activated in response to inflammatory disorder, or as a consequence of an immune reaction in vitro. Therefore, these cells play a vital role in the interaction between the immune system and VD, and their local production of $1,25(OH)_2D_3$ can affect other WBCs in a paracrine fashion[60].

Moreover, 1α-hydroxylase is not only expressed in normal tissue but also tumor tissue such as prostate and colorectal cancer[61,62]. After that, its expression was documented in other tumors such as the breast[63]. The parathyroid hormone is responsible for the tight regulation of the 1α-hydroxylase activity in the kidney and excessive rise in the levels of 1,25(OH) D3 is unable to cause hypercalcemia. Similarly, local production of VD analog by hydroxylation would not result in systemic hypercalcemia. In subjects suffering from secondary hyperparathyroidism (due to uremia), Correa *et al.* in 2005 suggested that the administration of non-1α-hydroxylated vitamin D analogs, which could be hydroxylated inside the parathyroid cells, result in an active VD receptor (VDR) binding compound with parathyroid hormone (PTH)-suppressive and antiproliferative actions[64]. Moreover, Segersten *et al.* in 2005 confirmed the expression of 1α-hydroxylase, 24-hydroxylase, and VDR in breast cancer cells and documented the activity of non-1α-hydroxylated VD analogs in tumor cells of the breast. These analogs could be used as a treatment choice for cancerous tissues in which 1α-hydroxylase is produced[63].

Vitamin D and cardiovascular disease (major cause of death in Libya)

Cardiovascular disease (CVD) is the major cause of morbidity and mortality in the Westernized world. Besides the well-known traditional risk factors for CVD, novel risk factors are coming out with promising therapeutic and prognostic roles. Among these factors, VDD has recently garnered a lot of attention and interest[65]. As discussed earlier, VD is implicated with a wide variety of chronic diseases, one of them being diabetes, which, when poorly managed, may lead to CVD. Nowadays, Cardiovascular diseases, such as coronary artery disease, heart failure, and atrial fibrillation, are often accompanied by a prevalent deficiency in VD. This deficiency has been linked to negative short and long-term prognoses[66].

In a recent randomized, double-blind, placebo-controlled trial of monthly VD (the D-Health Trial) in 2023, Thompson *et al.* investigated the effect of monthly VD supplementation on the incidence of major cardiovascular events in older people. The results showed that VD doses may reduce cardiovascular events, but the risk difference was small[67].

Cosentino *et al.* in 2021 concluded that despite the enhanced risk of CVD being associated with hypovitaminosis, experts are divided on whether it is simply an indicator of CVD or a contributing factor that can be treated. Similarly, they are uncertain if supplementing vitamin D in high-risk cardiovascular patients with insufficiency improves outcomes, and further investigation is required[66]. VD may reduce the risk of cardiovascular disease, suggests observational studies. A recent analysis of 34 publications with 180,667 participants found that increasing 25(OH)D levels by 25 nmol/l lowered the risk of CVD events and CVD mortality[68].

Recent reports suggest it seems that ischemic heart disease (IHD) is considered the first cause of death among the Libyan population. Furthermore, the rate of mortality due to IHD increased by 29.8 per 100,000 individuals in 2019 compared to the death rate estimated in 2009. The other causes of death are stroke, chronic kidney disease, hypertension, Alzheimer's disease, Lung cancer, and diabetes, respectively[69]. Normalization of VD by supplementation of VD may help in reducing the death rates as a consequence of IHD as well as the other causes of death. This suggestion is in agreement with the study of Pirrotta *et al.* in 2023, which suggested that low levels of 25OHD might indicate an increased risk of cardiovascular mortality[70].

Cardiovascular disease, including myocardial infarction, cerebral stroke, congestive heart failure, peripheral vascular disorders, and kidney disease, is significantly affected by hypertension, which is also considered the most common risk factor for CVD[71]. Studies have shown that reducing high blood pressure could lead to a 35% decrease in stroke incidents and an 18% decrease in heart attack occurrences[72,73].

In Canada, a recent study (belonging to the community-based program) evaluated 8,155 participants to examine the correlation between serum 25-hydroxyvitamin D [25(OH)D] status and blood pressure (BP), and the impact of vitamin D supplementation on hypertension. In this work, Mirhosseini *et al.* found that maintaining serum levels of 25(OH)D at or above 40 ng/mL in individuals with hypertension resulted in a significant reduction in systolic and diastolic blood pressure as well as mean arterial pressure[71]. The study also recommended that maintaining the desired serum levels of 25(OH)D, a daily intake of at least 4,000 IU/day (100 μg/day) of vitamin D is needed. The authors of the study concluded that encouraging lifestyle modifications, prescribing blood pressure-lowering medication, and supplementing with vitamin D may provide a straightforward, safe, and cost-effective approach to decreasing blood pressure in hypertensive individuals who are deficient in vitamin D[70].

Vitamin D and nonalcoholic fatty liver disease

Nonalcoholic fatty liver disease (NAFLD) is a condition characterized by the accumulation of fat in the liver without the presence of other factors such as viral hepatitis or alcohol abuse. It is considered a significant component of metabolic syndrome and has become a growing clinical concern[74]. NAFLD is the most common type of liver disease in adults, with a global prevalence of 32.4%[75,76]. The prevalence of NAFLD has increased rapidly over the past few decades. NAFLD is a term that includes the accumulation of benign adipose tissue in the liver, as well as progressive steatosis with hepatitis, fibrosis, cirrhosis, and hepatocellular carcinoma (HCC), and the patients have an increased risk of mortality compared with non-NAFLD individuals[77].

Animal studies have shown that VD can help regulate liver inflammation and fibrogenesis, as well as improve the liver's response to insulin[78]. Additionally, various cross-sectional and case-control studies have found an inverse association between NAFLD and serum 25(OH)D, which is a clinical marker for VD status[79,80]. In accordance with this, a recent observational, cross-sectional study was conducted over a span of 1.5 years (from January 2019 to June 2020) at the Department of General Medicine of a tertiary care hospital in northern India. The study involved 100 adult patients with NAFLD. The results showed that VDD increases the risk and severity of NAFLD. Determination of serum 25(OH)D levels can reduce NAFLD risk. Moreover, supplementing NAFLD patients with VD slows down the disease progression. VDD is also linked to abnormal liver enzymes and dyslipidemia in NAFLD cases[81].

Although the concentration of 25(OH)D was associated with NAFLD, Mendelian Randomization Analysis (MR analysis) suggested that there is no causal relationship between genetically determined serum 25(OH)D and NAFLD. Therefore, Wang *et al.* suggested that long-term VD deficiency may not affect the development of NAFLD[82]. On the contrary, a recent study by Yuan and Larsson found an inverse genetic association between serum 25(OH)D with NAFLD and liver enzymes and an inverse correlation of genetically predicted serum 25(OH)D with the risk of NAFLD in European populations. This research suggests that vitamin D might help prevent NAFLD, a liver disease. However, it is not yet clear whether NAFLD has a causal influence on reducing serum 25(OH)D, and thus more studies are needed to find out. Furthermore, the authors found that MR analysis reported a possible correlation of genetically predicted increased 25(OH)D levels with reduced concentrations of ALP and AST[83]. While ALP typically does not serve as a strong indicator for NAFLD, it is possible that the inverse associations observed with AST could suggest a protective function of elevated serum 25(OH)D levels in liver disease, specifically NAFLD. Moreover, vitamin D plays a crucial role in immune modulation, cell differentiation, and proliferation, as well as the inflammatory response, and could potentially affect the risk of NAFLD through these mechanisms[84].

Deficiency of VD leads to dysfunctional adipose tissue, resulting in chronic inflammation that could potentially cause the development of NAFLD[85]. Another study[86] reported that NAFLD patients had an unusual lipid metabolism and showed characteristics of metabolic syndrome. NAFLD is characterized by high levels of triglycerides, non-type A LDL, and low levels of HDL. It is caused by the excessive synthesis of very low-density lipoprotein by the liver and decreased clearance of lipids by the liver, leading to abnormal lipid metabolism. Insulin resistance drives the atherogenic lipid profile of NAFLD, which could be worsened by a lack of vitamin D.

Vitamin D and cancer

In 1980, the brothers Cedric and Frank Garland wrote an article about the importance of the production of VD via sun exposure, and this vitamin can reduce the risk of cancer in the large intestine (colon). The

manuscript was accepted and published in the UK in 1980[87]. After that, they found that consuming VD and calcium supported their hypothesis and caused a decrease in the risk of colorectal cancer[88]. A recent narrative review (by Muñoz and Grant, 2022) analyzed the results of ecological studies of cancer concerning indices of sun radiation and showed a decrease in the risk of incidence of cancer and death rates for about 23 types of cancer. Moreover, the analyses of observational studies reported that serum 25(OH)D was negatively correlated with the incidence of 12 types of cancer. The same source found no evidence that undiagnosed cancer decreases the serum levels of 25(OH)D except in advanced cancer stages. Regarding the analyses of serum 25(OH)D and cancer incidence, Muñoz and Grant in 2022 reported that increasing the serum levels to 80 ng/mL would decrease the incidence rates of cancer by 70% ± 10%[89]. In 2007, a meta-analysis included five case-control studies that reported a reduction in colorectal cancer by 50% ± 20% by achieving 34 ng/mL *vs.* 6 ng/mL[90].

Several studies have investigated the mechanisms by which VD exerts its positive actions on cancer cells. These underlying mechanisms were elegantly discussed in the narrative review by Muñoz and Grant, 2022, and these include inhibition of cellular proliferation in colon cancer[89], modulation of the immune system in the majority of cancers, sensitization of autophagy in colon cancer[91,92], and inhibition of cancer cell migration, invasion and metastasis as reported in prostate cancer[93-95].

Vitamin D also regulates some of the enzymes involved in the detoxification and xenobiotic metabolism in the liver and intestine. The xenobiotics metabolisms involve chemical reactions that finally lead to the elimination of foreign and toxic compounds and it includes two phases: phase I (hydroxylation oxidation and hydrolysis) followed by phase II (conjugation with many compounds such as glutathione) to increase the solubility of the xenobiotics to facilitate their excretion outside the body[96]. Collectively, these processes help fight cancer cells and also aid in the detoxification of anticancer drugs[97]. All these mechanistic influences confirm the multilevel anticancer roles of vitamin D. Therefore, the blood levels of VD should be maintained to reduce the risk and serious consequences of many cancers.

Vitamin D and the development of type 2 diabetes

During the previous decade, VDD was believed to increase the risk of type 2 diabetes (T2D), and supplementing VD was believed to lower the risk of diabetes. A meta-analysis of observational studies suggested that increasing the blood levels of 25 (OH) VD was linked to a reduction in the risk of T2D, especially among prediabetics[98].

The studies investigated the mechanism by which VD lowers the risk of T2D and suggested that VDD was linked to insulin resistance and a decrease in pancreatic β-cell function. Moreover, the supplementation of VD and calcium may improve insulin sensitivity and maintain β-cell function[99].

A recent clinical trial compared the influence of a daily supplement with 100 μg (4,000 units) of VD3 against placebo on the prevalence of new-onset diabetes in adult subjects with prediabetes. The exposure to VD was estimated as the cumulative rolling mean of annual serum 25(OH)D measurements. Daily consumption of VD and maintaining a serum 25(OH)D level at 100 nmol/l is a good intervention that finally led to a diminished risk of diabetes in adult prediabetics[100].

In another meta-analysis of 3 randomized trials of prediabetic individuals, the D2d trial evaluated the effect of taking 4,000 IU a day of VD3[101]. The other study was conducted in Norway (Tromsø trial)[102], which assessed the 20,000 IU-bolus doses of VD3 per week (about 3,000 IU/day). The third one was a subset trial from Japan that analyzed a synthetic analog of a VD[103]. All of the trials had similar duration (about 3 years).

The hazard ratio in the meta-analysis was 0.88, indicating a moderate risk decrease that just met statistical significance.

A recent work (the VITAL trial) showed that making modifications to the BMI had a positive impact on VD for autoimmune diseases, total invasive cancer, cancer death, and others. The study reported that for individuals who had a BMI below 31, there was a significant (24%) decrease in risk, while those with a BMI of 31 or more had no decrease in risk[104].

Regarding the synthetic analog trial, the hazard ratio was similar to that of other trials; however, there was no modifying effect of BMI. The study suggested that this is due to VD3 (cholecalciferol) requiring conversion to 25-(OH) D in the liver and other tissues and that the CYP2R1 is influenced by BMI. There is some evidence that CYP2R1 expression can be upregulated by weight loss, so a rise in BMI may actually interfere with the ability to activate 25-(OH) D to the active form [1,25-(OH) VD]. So, we need more research in terms of the safety of long-term use of VD at these higher doses. It is necessary to compare these results with those of the Diabetes Prevention Program trial, which also tested the prediabetics. Lifestyle changes led to a 58% decrease in T2D, and in the case of metformin, the reduction in T2D was about 31%, which was much larger than that seen with high-dose VD. Based on these findings, Dr Manson suggested that it is necessary to focus on modifying the lifestyle to avoid diabetes[105].

Vitamin D and COVID-19 infections

Observational studies reported a link between reduced serum VD levels and the severity of COVID-19 infections and mortality rates[106]. Moreover, non-randomized observational studies documented the advantages of using VD supplements in subjects suffering from COVID-19[107]. Recent evidence suggested that VD supplements could facilitate immune responses to the vaccines used for COVID-19[108]. Moreover, the Co-VIVID study concluded that increasing the serum levels of VD was linked to a significant reduction in rates of COVID-19-related conditions. On the other hand, no significant difference was observed in the relative risk of admission to intensive care units (ICU) and mortality rates as a result of the consumption of VD supplements[109].

Recent mechanistic reports showed that VD could stimulate immunomodulatory effects of both arms of the immune system (innate and adaptive immune responses), stimulate the synthesis of antiviral factors, and play an anti-inflammatory role. Furthermore, VD could influence the gene expression of COVID-19 and reduce the severity of the infection via the binding of VD to the response element of VD in the DNA[110].

Previous studies have clearly demonstrated the important benefits of the use of VD in the management of COVID-19 condition. Maintaining the serum levels of VD through supplementation helped in improving the body's susceptibility to COVID-19 infection, alleviated the severity of the symptoms of the disease, and decreased the probability of patient admission to the ICU, and these benefits led to a reduction in the mortality rates associated with the infection and its related health conditions.

Vitamin D and pregnancy

It is well established that the period of pregnancy is the hardest time for every woman. Internal and external factors may influence the growing embryo, which may cause unfavorable conditions in the future life of the offspring. Among these factors is the VD [25(OH) D] status of the mother, whose deficiency during pregnancy was associated with health conditions including preeclampsia[111], gestational diabetes[112]., bone-related disorders, increased rate of cesarean delivery, and preterm birth[113].

A recent work by Rostami *et al.* aimed to determine the effectiveness of a prenatal screening program in optimizing 25-25(OH)D levels and preventing pregnancy complications. The screening and non-screening arms of the study were carried out in two cities from Khuzestan province, Iran, namely Masjed-Soleyman and Shushtar, respectively. In the screening arm, a randomized controlled trial involving 800 pregnant women was conducted. This research work found that after taking supplements, a mere 2% of women at the non-screening site achieved the required level of sufficiency (> 20 ng/mL), whereas 53% of women belonging to the screening arm reached the desired level. Moreover, in the screening arm, adverse pregnancy outcomes, such as preeclampsia, gestational diabetes mellitus, and preterm delivery, decreased by 60%, 50%, and 40%, respectively. The authors also cautiously conclude that doses of 300,000 IU for moderately deficient women and 600,000 IU (divided into two doses) for severely deficient women, followed by monthly maintenance therapy (50,000 IU)[114].

Many cross-sectional studies reported that maternal VDD is common during the period of pregnancy. Despite the availability of sunshine during the four climate seasons, pregnant women in Mediterranean countries experienced a high prevalence of VDD[115]. The prevalence of VDD or insufficiency, at the least, ranges from 40% to 90% among pregnant women in Spain and Turkey, and vitamin D insufficiency or deficiency occurs in up to 41% and 90%, respectively, of pregnant populations[116,117]. These studies were in agreement with recent work in the city of Misurata (Western Libya), in which 90 pregnant women (most of them aged 15-25 years) were included in a descriptive research work in March 2018. The study reported a high prevalence of 25(OH) D insufficiency (> 50%) among pregnant women, despite the enhanced awareness of the benefits of VD in recent times and although VD supplements are generally prescribed during pregnancy[118]. Accordingly, a study was conducted to assess the prevalence of VDD during the second trimester of pregnancy among 300 women (mean age 34,6 years and age range 20-40 years) in Alkhoms City (Western Libya). The results indicated that VDD was closely associated with women at age 40 years. The study showed a prevalence of 38% of VDD and 62% of VD insufficiently, and all the subjects were in the age ranges between 20 and 30 years[119].

A systematic review (2016) analyzed serum levels of 25(OH)D in pregnancy in Mediterranean countries and evaluated the main predictors of reduced 25(OH)D values in the Mediterranean paradox. The authors reported that the prevalence of VDD differed widely and ranged from 22.7% to 90.3%, whereas that of VD insufficiency was from 9.3% to 41.4%. Furthermore, the study found a positive correlation between 25(OH)D levels and light skin color, white race, uncovered dressing pattern, maternal VD supplementation, and season of gestation (spring/summer), and a negative correlation between VD levels and BMI and gestational age. The authors concluded that VDD among pregnant women showed a high prevalence in the Mediterranean countries. Racial, social, and cultural habits, as well as the lack of VD supplementation and dietary planning to maintain VD levels, seem to alleviate the advantages and benefits of exposure to sunshine[115].

Effects of VD supplements on health conditions and how much VD needed

For a long time, VD has been perceived as a magic solution and can be beneficial in many chronic illnesses ranging from general fatigue to cancer. Many of the findings related to this issue were obtained from observational research in which the rise in serum VD levels was related to a reduced risk for these conditions[120].

“Correlation doesn't prove causation” that is what we have gained from epidemiology science. Other factors may have an effect; for example, individuals who have increased levels of VD may consume healthier foods stuff, or they may stay longer periods exposed to sunshine, or do enough exercise. A collection of these

factors, or at least a few of them, could be involved in reducing their risk for these health conditions. After that, many of the randomized trials found no influence of the administration of higher doses of VD upon the wide variety of these disorders (including diabetes, cognitive decline, depression, cardiovascular disease, cancers, and even bone disease)[121].

Recent trials reported that small and moderate doses of VD (400-800 IU daily or 2,000 IU daily as applied in the VITAL trial) have not proven a decrease in many health outcomes. The VITAL study has generally not shown reductions in the major health outcomes. Two exceptions were reported in VITAL, including a 22% decrease in autoimmune disorders[122] (such as rheumatoid arthritis and psoriasis) and a 17% reduction in late-stage cancers[123].

Dr JoAnn Manson, professor of medicine at Harvard Medical School, as a director of the VD and Omega-3 trial (VITAL), the largest randomized clinical trial in the world, suggested that adult individuals need only small to moderate amounts of VD to meet the need for VD for bone health and many other outcomes. There are a few exceptions including patients in nursing homes who may have diets that are poor in VD and limited time out of doors. For people with malabsorption conditions and those with osteoporosis, it is still quite reasonable to prescribe calcium and VD. It is necessary to focus on implementing healthy changes in lifestyle for the prevention of type 2 diabetes and other metabolic diseases. Additional research on the safety of high doses of VD will be essential[121].

The possible causes of VD Deficiency and actions needed to improve VD status among Libyan population

Normal serum VD levels play a pivotal role in preventing the occurrence of Rickets, osteomalacia, and other VDD-associated disorders. Normalization of the levels of VD in the blood could be achieved by exposing the face and arms to direct sunlight for at least 25 min on three occasions during the 7 days of the week starting at 9 a.m.[124]. The reduction in serum VD levels in females in Libya and Middle Eastern areas, despite the sun shining being present mostly all the times of the year, may be due to wearing outdoor traditional Islamic clothes that cover most of the body, based on religious instructions.

In Libya and other Islamic countries in the Middle East, there are two styles of dressing: the first one is called Hijab, which covers the whole body of a woman except the face and hands, and the second style is called the Niqab, which covers all the body, including the face. These styles provide a reasonable explanation for the elevated prevalence of VDD among adult females in Libya and other Arabic countries. Moreover, this way of dressing caused a decrease in photosynthesis of VD by preventing the direct exposure of sunlight to the skin. This conclusion was supported by the findings of Al-Graiw *et al.*, who reported a reduced serum VD in Libyan females in the capital Tripoli compared with the VD values in women wearing Westernized style dressing[30]. Further support comes from the study of Perampalam *et al.*, who found an elevation in VD production with the heightened exposure of larger areas of skin to sunshine radiations[125].

Moreover, the high prevalence of VDD in the southern region of the country could be due to the fact that the vast majority of the inhabitants of this area have dark skin, which represents a barrier that resists the skin penetration of the sun radiation, thus reducing the production of VD. Correspondingly, previous studies have documented that skin color is one of the factors that could affect VD status[126]. Pregnant women with darker skin had a higher risk of having VDD than their white counterparts. This suggestion is supported by previous studies documented that black, Asian, and Hispanic races were more prone to VDD[127].

On the other hand, recent work showed that VD supplementation (10 ng/day) for pregnant women in Libya did not alleviate the status of VDD[119]. Consistently, other research studies have shown that the significant effects of vitamin D status are possibly achieved due to lifestyle modifications in developing countries[128,129]. The explanation for these findings comes from the evidence that dietary sources can supply only a minor proportion (20%) of the total need for VD by humans[7]. VD is obtained, in the first place, by synthesis beneath the skin. About 80% is obtained through the effect of ultraviolet B radiation from direct exposure to sunlight. Thus, sun exposure is primarily responsible for preventing VDD[130,131].

It is well established that Melanin has vital effects on maintaining health. It influences the under-skin synthesis of VD. Melanin determines the degree of pigmentation of the skin and protects it from the adverse effects of ultraviolet light. Synthesis of VD beneath the skin is dependent on ultraviolet-B light. African-origin individuals are characterized by excessively pigmented skin, which represents a barrier that resists most ultraviolet-induced VD synthesis. These individuals are advised to have VD supplements to normalize their blood levels of VD[132].

Among the contributing factors for hypovitaminosis D are female gender, older age, obesity, and low consumption of VD-rich foods[133]. Individuals suffering from obesity may have reduced serum VD levels because it is a fat-soluble vitamin that can be sequestered and stored in adipose tissue, thus reducing VD bioavailability in the bloodstream which further affects its physiologic functions[134].

CONCLUSION

In this review, we illustrated that the prevalence of VDD and severe VDD conditions are high in various parts of Libya, which was also comparable to Middle East regions and the entire world. These conditions represent a big challenge for people who work in the Ministry of Health. However, the causes of the higher incidence rates of VDD have not been fully clarified. VD research showed that the causes of VDD include lower exposure to sun radiation, wearing clothes that cover most parts of the body, sedentary and indoor working styles, and consuming foods poor in VD. Research believes that VD deficiency is associated with a wide variety of health problems, including bone disease, autoimmune disease, cardiovascular diseases, diabetes, and cancer. Our results indicate that VD deficiency represents an important public health issue in Libya. This work advised that the health authorities in the country should consider conducting a representative national nutrition survey to assess the mean/prevalence levels of VDSP standardized serum 25(OH)D by age, sex, region, and education/income. These findings encourage health professionals to take preventive actions to deal with the high prevalence of VDD to avoid the higher incidence of unfavorable health complications linked to this condition.

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Author's Contribution

The author contributed solely to the article.

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