MINI-REVIEW article

# Analysis of the association of vitamin D<sub>3</sub>, hemoglobin and ferritin with special respect to Libyan patients

### Salsabil A. Ansari<sup>1</sup>, Rana A. Boker<sup>1</sup>, Mariam S. Alsaid<sup>1</sup>, Roba F. Sherif<sup>2</sup> and Fathi M. Sherif<sup>1\*</sup> 🖾 🗓

<sup>1</sup> Department of Pharmacology and Clinical Pharmacy, Faculty of Pharmacy, University of Tripoli, Tripoli, Libya <sup>2</sup> Department of Pharmacology, Faculty of Medicine, University of Tripoli, Tripoli, Libya <sup>\*</sup>Author to whom correspondence should be addressed

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Abstract: Anemia, iron deficiency and iron deficiency anemia are common blood disorders. The role of vitamin D was agreed to be regulating calcium and phosphate absorption and bone metabolism and its deficiency is observed as a crucial nutritional problem. Vitamin D is created under the skin by ultraviolet light. It is usually getting vitamins from the food; however, in the case of vitamin D, there simply are not enough rich food sources for people to get adequate amounts in their diet. Its effects on the prevention of diseases such as cardiovascular disease and anemia have received much attention recently. To get sufficient vitamin D, need to be exposed to sunshine or use supplements. Vitamin D<sub>3</sub> was found in the largest population as a deficiency. With regard to hemoglobin the subject who has a less normal range of hemoglobin (19.05%) than the international normal range, and in ferritin the low population number was the subject whom has less normal range of ferritin than WHO normal range. The population that has low ferritin also has low vitamin D<sub>3</sub> and variable hemoglobin. According to international guidelines, optimizing nutrition with daily or intermittent (1 to 3 times per week) iron supplementation, should be considered a first-line intervention in high-risk or high-prevalence groups. Although it is probably less effective than daily iron supplementation, intermittent iron appears to be a useful and cost-effective way of controlling anemia and iron deficiency anemia. This may indicate a positive relation between the low concentration parameter of vitamin  $D_3$  and ferritin level but no significant correlation with hemoglobin.

# Introduction

Vitamin D is created under the skin by ultraviolet (UV) light and turned into a hormone in the body [1]. All cells, tissues and organs in the human body have vitamin D receptors. The most basic and best-known role of vitamin D is to regulate calcium phosphorus metabolism [1]. Low levels of calcium affect the central nervous system and also the cardiovascular system [1]. As such, the level of synthesis is influenced by a number of factors, including season of the year, skin pigmentation, and latitude, use of sunscreen, clothing and amount of skin exposed. Age is a factor, in that synthesis of vitamin D declines with increasing age, due, in part, to alteration in skin morphology [2]. Its use may well prevent several degenerative diseases and it may play a role as an anticancer agent [4]. Vitamin D<sub>3</sub> is converted to 25-hydroxyvitamin D (250HD) in the liver by a number of enzymes of which CYP2R1 is the most important [5]. The major effects of vitamin D<sub>3</sub> are to increase the active absorption of calcium from the proximal intestine and to bring about the mineralization of

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bone [6]. According to several studies, elderly men and women are deficient in vitamin D [3]. More than 50% of postmenopausal women taking medication for osteoporosis had suboptimal levels of 25OHD [3]. Children and young adults are potentially at high risk for vitamin D deficiency. 52% of Hispanic and black adolescents and 48% of white preadolescent girls had low 25OHD levels. People living near the equator who are exposed to sunlight without sun protection have robust levels of 25OHD [3]. Also at risk are pregnant and lactating women, 73% of the women and 80% of their infants were vitamin D-deficient at the time of birth [3]. However, even in the sunniest areas, vitamin D deficiency is common when most of the skin is shielded from the sun. Saudi Arabia, the United Arab Emirates, Australia, Turkey, India and Lebanon, 30% to 50% of children and adults had low 25OHD levels under 20 ng per milliliter [3]. The major cause of vitamin D deficiency is inadequate exposure to sunlight [9].

Vitamin D deficiency causes muscle weakness affected children have difficulty standing and walking, whereas the elderly have increasing sway and more frequent falls, thereby increasing their risk of fracture [9], schizophrenia and depression [10]. Infections such as tuberculosis, urinary tract infection, asthma and wheezing diseases [10], High blood pressure and coronary heart disease, also, adult-onset diabetes mellitus [10], Type 1 diabetes, multiple sclerosis, rheumatoid arthritis, Crohn's disease [10]. There is an inverse association between serum 25OHD and body mass index greater than 30 kg per m<sup>2</sup>, and thus, obesity is associated with vitamin D deficiency [9]. Patients on a wide variety of medications, including anticonvulsants and medications to treat AIDS/HIV are at risk because these drugs enhance the catabolism of 25OHD and 1,25(OH)2D [9]. Ferritin, an iron storage protein, is the primary iron storage mechanism and is critical to iron homeostasis. Ferritin makes iron available for critical cellular processes while protecting lipids, DNA and proteins from the potentially toxic effects of iron. Alterations in ferritin are seen commonly in clinical practice, often reflecting perturbations in iron homeostasis or metabolism. It is increasingly recognized that ferritin plays a role in multitude of other conditions, including inflammatory, neurodegenerative and malignant diseases [13]. The subunits are of two types, termed H and L. The ratio of these subunits varies widely depending on tissue type and can be modified in inflammatory and infectious conditions. Ferritin serves as a critical component of iron homeostasis. Its primary role is in iron sequestration in which it functions as a ferroxidase, converting Fe(II) to Fe(III) as iron is internalized and sequestered in the ferritin mineral core [13]. Iron is toxic in cellular systems because of its capacity to generate reactive species which can directly damage DNA and proteins. Ferritin captures and buffers the intracellular iron pool and thus is a key component in organism survival. Homozygous murine knockouts of ferritin H are lethal [13]. Several iron disorders that affect movement and other neurologic functions have been characterized (Parkinson's disease, Friedreich's ataxia, neuroferritinopathy, ferritin cataract syndrome-ferritin L hyperferritienemia and restless legs syndrome) and those whose pathophysiology is most directly linked to abnormalities in ferritin. The normal range as sufficient blood concentration of vitamin D<sub>3</sub> must be between 30-60 ng per ml in male and female subjects. Table 1, vitamin D3 the largest population number who has a deficiency compared to the population whom has sufficient vitamin D3 concentration, which may contribute to many explanations inadequate exposure to sunlight, wearing a sunscreen with a sun protection factor of 30 reduces vitamin D synthesis in the skin, people with a naturally dark skin tone have natural sun protection and require at least three to five times longer exposure to make the same amount of vitamin D as a person with a white skin tone, food, age, pregnancy, obesity, different seasons, geographic area, patients with one of the fat malabsorption syndromes and bariatric patients are often unable to absorb the fat-soluble vitamin D, and patients with nephrotic syndrome lose 25(OH)D bound to the vitamin D-binding protein in the urine, patients on a wide variety of medications, including anticonvulsant drugs and medications to treat AIDS/HIV, are at risk because these drugs enhance the catabolism of 25(OH)D and 1,25(OH) 2 D and secondary hyperparathy-roidism maintains serum calcium in the normal range at the expense of mobilizing calcium from the skeleton and increasing phosphorus wasting in the kidneys.

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The total hemoglobin levels in Libyan patients showed low concentration and had the lowest mean and the high concentration parameter had the highest mean (Table 2). The mean values of the Libyan study are within the WHO normal ranges and the mean value of hemoglobin in a low group is less than the WHO normal range. The mean value of hemoglobin in a medium group of this study is 13.46 within the WHO normal range and the mean value of hemoglobin in the high group is also within the WHO normal range (Table 2). With regard to gender, the male has a high mean value of 55.0% and the female group has a low mean of 45.0% which is in line with WHO normal ranges. The adult group has a low mean value of 13.66 with 47.88%, the adolescence group has the highest mean value of 15.08 with 32.0% and the children group has a mean value of 11.64 with 20.4%. This is in line with WHO's normal ranges. With regard to total ferritin, the low concentration parameter has the low mean value of 8.51 and a smaller number of patients, the medium concentration parameter has the highest mean value of 72.371 and no high concentration values (Table 3). In a recent study, Yoon et al. [14] reported vitamin D has positively been associated with serum ferritin levels in Korean women without metabolic syndrome but not in women with metabolic syndrome. However, more recently, supplementation with vitamin D had no significant effect on hemoglobin and ferritin levels while positive effects on transferrin saturation and iron status were reported [15]. The authors have recommended Further clinical studies to determine the actual effect of this intervention on hemoglobin levels. A low population number who have less normal range of hemoglobin than the WHO normal range, thus, causes anemia which may contribute to physical (blood loss as trauma), diseases such as acute or chronic gastrointestinal hemorrhage: secondary to ulcer, inflammatory bowel disease, tumor or infection. In addition, intraoperative blood loss and excessive phlebotomy, renal disease, erythropoietin deficiency, endocrine disorder (thyroid and pituitary disease) and chemical (toxicity by heavy metal). In ferritin, the low population number who have a less normal range of ferritin than WHO's normal range, thus, may contribute to diet, lifestyle and diseases. Less variation in samples taken (age, gender, weight, diseases and environmental factors). This may support a positive relation between the low concentration parameter of vitamin D<sub>3</sub> and ferritin level and no correlation with hemoglobin level.

Parameters		Mean	Number	Range
Concentration	Deficient	11.31	45	03.90 - 19.2
	Insufficient	24.93	10	02.00 - 29.3
	Sufficient	37.33	06	33.18 - 46.4
Gender	Male	14.75	17	07.0 - 29.3
	Female	21.15	44	11.0 - 46.4
Age class	Child	12.46	06	08.0 - 27.8
	Adolescence	13.15	16	06.0 - 22.7
	Adult	17.22	39	03.9 - 46.4

Table 1: Vitamin D<sub>3</sub> levels in Libyan subjects

Parameters		Mean	Frequency	Range
Concentration	Low	11.075	04	09.2 - 12.0
	Medium	13.46	13	12.3 - 15.6
	High	16.50	04	16.0 - 16.7
Gender	Male	14.85	11	12.0 - 16.0
	Female	12.90	10	09.2 - 13.9
Age class	Children	11.64	05	09.2 - 12.7
	Adolescence	15.083	06	12.4 - 16.7
	Adults	13.66	10	11.5 - 16.7

Parameters		Mean	Frequency	Range
Concentration	Low	8.513	09	02.4 - 10.6
	Medium	72.371	35	12.55 - 173.9
	High	-	-	-
Gender	Male	92.570	13	09.0 - 293
	Female	45.349	31	02.4 - 247
Age class	Child	21.424	05	06 - 50
	Adolescence	53.547	11	10.6 - 119
	Adults	68.325	28	02.4 - 293

**Table 3:** Total ferritin levels in Libyan subjects

*Conclusion:* This review concludes that vitamin  $D_3$  has no clear influence on hemoglobin and ferritin while positive effects on transferrin saturation and iron status were reported. Thus, more studies are needed to determine the actual effect of this relation on hemoglobin levels.

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**Ethical issues:** Including plagiarism, informed consent, data fabrication or falsification and double publication or submission completely observed by the authors.

**Data availability statement:** The raw data that support the findings of this article are available from the corresponding author upon reasonable request.

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