

Vitamin D, optimal health and athletic performance: A review study

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Abstract: Background: Vitamin D, also known as calciferol, is a secosteroid hormone and an essential nutrient responsible for multiple biological functions in the human body. Functionally it is different from all other fat soluble vitamins. The body can synthesis it with the help of sunlight. Objective of the Study: The specific objective of this review article is to explore the emergence of vitamin D as an important nutrient for the maintenances of optimal health and athletic performance. Acquisition of Evidence: Evidences were gathered through Pubmed searching. Studies directly matched and fulfill the primary objective of this article were considered, reviewed properly and presented systematically. Findings: Commonly Vitamin D is well recognized for its active role in calcium and phosphorous homeostasis in the human body. In recent era scientists have identified that almost every cell in the body express the vitamin D receptor, physiologically play a significant role in achieving optimal health and better athletic performance. Active from of Vitamin D plays an important role for the prevention of many chronic diseases including cancer, cardiovascular diseases, autoimmune diseases, diabetes, arthritis etc. Conclusion: Vitamin D is a potent nutrient and working as a regulator of several physiological functions in the human body. Some of these functions are well recognized but many are yet to be researched to understand the complete mechanism of action as it plays in the human body.

Keyword: Prohormone, Conditional Vitamin, Sleeper Nutrient, Sports Performance

1. Introduction

Vitamin D is a sleeper nutrient. Vitamin D was classified as a vitamin in the early 20th century and in the second half of the 20th century as a prohormone (“conditional” vitamin) [10, 11]. There is a growing awareness that vitamin D is an essential nutrient required for optimal health. A recent trend in vitamin D research suggests that it is vital in different bodily biological functions, reaching optimal health and better athletic performance. The specific objective of this article is to explore the emergence of vitamin D as an important nutrient for the maintenances of optimal health and athletic performance.

2. Source of Vitamin D

The main source of vitamin D for humans is exposure to sunlight. Our skin is the active site for vitamin D synthesis, 90–95% of most people’s vitamin D requirement comes from casual sun exposure. Very little vitamin D is naturally present in our food. Oily fish including salmon, mackerel, and herring; cod liver oil; and sun-dried mushrooms typically provide 400–500 IU of vitamin D per serving. The major foods that are fortified with vitamin D include milk, orange juice, cereals, some bread, some yogurts and cheeses are the dietary source of Vitamin D [25, 60].

3. Vitamin D Synthesis and Mechanism of Action

Vitamin D, also known as calciferol, is a fat soluble vitamin. It is different from all other fat soluble vitamins. The body can synthesis it with the help of sunlight. There are two forms of vitamin D, vitamin D₃ (cholecalciferol), which is produced from the conversion of 7-dehydrocholesterol in the epidermis and dermis in humans, and vitamin D₂ (ergocalciferol) which is produced in mushrooms and yeast. The efficiency of the conversion of 7-dehydrocholesterol to vitamin D₃ is dependent on time of day, season of the year, latitude, skin color and age. Vitamin D is not biologically active, the active form is 1,25-dihydroxyvitamin D [1,25(OH)₂D]. Synthesis of vitamin D takes place in several different steps (Figure 1). The synthesis of vitamin D starts in

the bowel epithelial with the oxidation of cholesterol from food or bile to pro- vitamin D₃ (7-dehydrocholesterol), a precursor of cholesterol, which is then transported to the skin, mainly the epidermis, wherein it is isomerized to pre-vitamin D₃ (cholecalciferol) by UVB radiation [8]. Once vitamin D is made in the skin or ingested from the diet, it travels to the liver where it is converted to 25-dihydroxyvitamin D [25(OH)₂D]. This major circulating form of vitamin D is then converted in the kidneys to its active form 1,25-dihydroxyvitamin D [1,25(OH)₂D]. 25-hydroxyvitamin D has low biological activity, but it is the major form of vitamin D that circulates in the blood stream. Serum 25(OH)D concentrations are generally thought to reflect nutritional status. The measurement of the major circulating form of vitamin D, 25(OH)D, is the gold standard for determining the vitamin D status of an individual [19, 29].

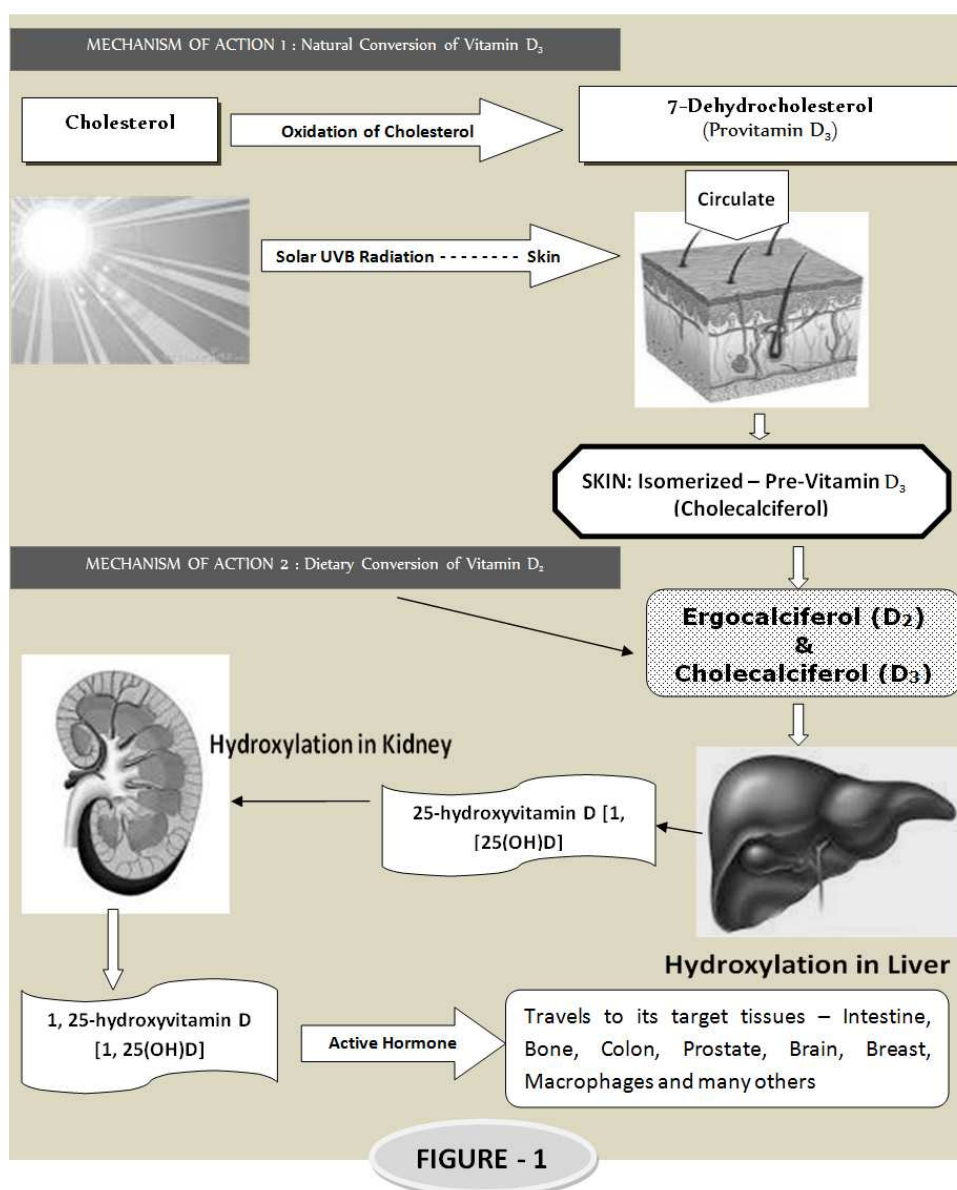


Figure 1. Chemical Conversion of Vitamin D and Mechanism of Action

As stated above vitamin D is metabolized in the liver to 25-dihydroxyvitamin D [25(OH)₂D] and then in the kidneys

to 1,25-dihydroxyvitamin D [1,25(OH)₂D]. 1,25-dihydroxyvitamin D produced by the kidneys enters the

circulation and travels to its major target tissues the intestine and bone, where it interacts with its vitamin D receptor to enhance intestinal calcium absorption and mobilize osteoclastic activity (Figure 1). It is also recognized that many other tissues in the body, including macrophages, brain, colon, prostate, breast, and others, have the enzymatic machinery to locally produce 1,25(OH)₂D [18, 48, 61].

4. Vitamin D Deficiency – A Pandemic

Vitamin D deficiency is a worldwide problem and usually accepted by the scientists of all over the world. Vitamin D deficiency is manifested as rickets in children and as osteomalacia in adults. Lack of this vitamin in adults may

also contribute to the development of osteoporosis [29-31, 34, 35].

Much debate has taken place over the range of vitamin D deficiency. Vitamin D deficiency is opined by most experts as a 25-hydroxyvitamin D [25(OH)D] level of less than 20 ng per milliliter (50 nmol per liter). A level of 25-hydroxyvitamin D of 20 to 30 ng per milliliter (50 to 80 nmol per liter) can be considered to indicate a relative insufficiency of vitamin D, and a level of 30 ng per milliliter or greater can be considered to indicate sufficient vitamin D level. Whereas, Vitamin D intoxication is observed when serum levels of 25-hydroxyvitamin D are greater than 150 ng per milliliter (374 nmol per liter) [20, 25, 49, 60].

Table 1. Health Implications of Various Levels of Serum 25(OH)D

25(OH)D Level (ng/ml)	25(OH)D Level (nmol/L)	Health Implications
<20	<50	Deficiency
20 – 30	50 – 80	Insufficiency
30 – 100	80 – 250	Sufficiency
54 – 90	135 – 225	Normal in Sunny Countries
>100	>250	Excess
>150	>325	Intoxication

5. Vitamin D and Optimal Health

Recent research reports strongly agree that Vitamin D sufficiency is required for optimal health [6, 10]. There are good reasons that vitamin D sufficiency be maintained during all stages of life, from fetal development to old age [21, 56]. Therefore the importance of vitamin D sufficiency throughout the life is discussed in the following.

5.1. Pre and Postnatal Vitamin D Benefits

The sufficient amount of vitamin D is especially important during pregnancy and lactation because bones develop rapidly in this period. Insufficient vitamin D intake during infancy can result in biochemical disturbances, reduced bone mineralization, slower growth, bone deformities, and increased risk of fracture – the hallmarks of rickets. Low birth weight (LBW) appears to be a consequence of vitamin D insufficiency during pregnancy which disrupted calcium homeostasis, leading to intrauterine growth retardation, premature labor, and hypertension, all of these are risk factors for LBW infants. Children born prematurely are likely to have enamel defects in both primary and permanent teeth. Maternal vitamin D sufficiency is required for proper fetal tooth development as well as adequate calcium. Maternal and infant sufficiency of vitamin D also appears to greatly reduce the risk of type 1 diabetes mellitus (DM) and multiple sclerosis (MS) [11, 27, 39].

5.2. Vitamin D Benefits during Youth and Adolescence

The primary role of sufficient vitamin D during youth and adolescence is essential for bone mineral density and other

musculoskeletal growth [10, 11, 27].

5.3. Vitamin D Benefits in Adulthood

Vitamin D levels in adulthood are important for maintaining bone mineral density and optimal muscle function. Evidence suggests that sufficient vitamin D levels in adulthood may significantly reduce the risk for many types of cancer, multiple sclerosis and tuberculosis [9-11].

5.4. Vitamin D Benefits in the Elderly Populations

The elderly have a particularly strong need to maintain vitamin D sufficiency. Not only are they likely to produce less vitamin D from solar UVB irradiation because they generally spend less time in sunlight than do younger people, but their efficiency of photoproduction is less. In addition, diseases such as cancer and osteoporotic fractures are most likely among the elderly [9-11, 13].

6. Biological Significance of Vitamin D

The biological function of vitamin D in the human body is diverse. For example, as recently noted, 1,25(OH)₂D inhibits parathyroid hormone (PTH) secretion and promotes insulin secretion, inhibits adaptive immunity and promotes innate immunity, and inhibits cell proliferation and stimulates their differentiation. The main biological function of vitamin D in humans is to maintain normal blood levels of calcium and phosphorus. This in turn sustains the normal mineralisation of bone, muscle contraction, nerve conduction and general cellular function in all cells of the body. Directly or indirectly, 1,25-dihydroxyvitamin D controls more than 200 genes,

including genes responsible for the regulation of cellular proliferation, differentiation, apoptosis, and angiogenesis [42]. The active form of vitamin D [1,25-dihydroxyvitaminD] or calcitriol, also regulates the transcription of a number of vitamin D-dependent genes coding for calcium transporting proteins and bone matrix proteins. The most tissues and cells in the body, including those of the liver, pancreas, colon, osteoblasts, brain, heart, lung, breast, gonads, prostate, skin, muscle, adipose tissue, macrophages and activated T and B lymphocytes [15] have a vitamin D receptor (VDRs). Active form of vitamin D plays an important role in decreasing the risk of many chronic illnesses, including common cancers, autoimmune diseases, infectious diseases, and cardiovascular disease [30, 48, 51].

It appears from the epidemiological, clinical and experimental observations that Vitamin D plays a vital role for overall health and wellbeing throughout the life. The complete physiological mechanism of Vitamin D is not understood properly but scientists working with Vitamin D constantly reported that it is a potent nutrient which controls many biological functions in the body. Therefore the overall biological significance and recognized physiological actions of vitamin D in the human body are discussed here for further understanding.

6.1. Vitamin D and Adiposity

Recent research suggests that excess adiposity may increase risk for low vitamin D status. A lower serum 25(OH)D concentration and a higher serum parathyroid hormone concentration were observed in obese subjects compared with nonobese subjects suggesting that the larger body fat compartments in the obese individuals sequester vitamin D. In obese subjects exposure to the same amount of UV radiation raised plasma 25(OH)D concentration by only 50% compared with non-obese subjects. The content of the vitamin D₃ precursor 7-dehydrocholesterol in the skin was not significantly different between obese and non-obese subjects and the percentage conversion to previtamin D₃ and vitamin D₃ was similar in both groups. Obesity did not, therefore, affect the capacity of the skin to produce vitamin D₃, but may have altered the release of vitamin D₃ into the circulation, due to more being deposited in subcutaneous fat in obese subject [27, 55].

6.2. Vitamin D and Bone Health

Vitamin D is essential for natural bone metabolism. Without vitamin D, only 10 to 15% of dietary calcium and about 60% of phosphorus is absorbed. The interaction of 1,25-dihydroxyvitamin D with the vitamin D receptor increases the efficiency of intestinal calcium absorption to 30-40% and phosphorus absorption to approximately 80%. Vitamin D supplementation improved osteoporosis and reduce bone fractures in the elderly [30]. Vitamin D maintains calcium and phosphorus homeostasis which impacts on cellular metabolic processes and neuromuscular functions. Vitamin D promotes calcium absorption in the

gut and maintains adequate serum calcium and phosphate concentrations to enable normal mineralization of bone and to prevent hypocalcemic tetany. It is also needed for bone growth and bone remodeling by osteoblasts and osteoclasts activity. Without sufficient vitamin D, bones can become thin, brittle, or misshapen. Vitamin D sufficiency prevents rickets in children and osteomalacia in adults. Together with calcium, vitamin D also helps protect older adults from osteoporosis. Vitamin D also facilitates the absorption of intestinal phosphate. 1,25(OH)₂D, in concert with parathyroid hormone, also causes demineralization of bone when calcium concentrations fall to maintain plasma concentrations within a narrow range. It has yet to be determined whether 1,25(OH)₂D directly influences bone mineralization [12, 38].

6.3. Vitamin D and Muscle Function

In recent decades, there has been increased awareness of the impact of vitamin D on muscle morphology and function. Both cross-sectional and longitudinal studies allude to a functional role for vitamin D in muscle and more recently after the discovery of the vitamin D receptor (VDR) in muscle tissue provides a mechanistic understanding of the function of vitamin D within muscle [3, 5, 16].

In general it has been reported physical performances, neuromuscular function, muscle strength, myopathy, muscle weaknesses, postural sway, gait disturbances and an increased risk of falls in elderly subjects are associated with vitamin D insufficiency. [22, 51]. In several studies, physical activity has been shown to correlate positively with vitamin D status which most likely is due to the fact that physically active subjects spend more time outdoors in the sun and accordingly have a higher endogenous vitamin D synthesis than physically inactive subjects. Similarly vitamin D supplementation improved neuromuscular function, muscular strength and weaknesses [14, 15].

However, independent effect of vitamin D on muscle function is still debatable rather its impact was felt to be indirect [22]. The active form of vitamin D [1,25(OH)₂D] and the VDR influence skeletal muscle via both genomic and nongenomic mechanisms. The binding of 1,25(OH)₂D to the VDR results in enhanced transcription of a range of proteins, including those involved in calcium metabolism. Calcium is a critical modulator of skeletal muscle function and any perturbation to calcium handling may impact on both its contractile and relaxation properties. Therefore, 1,25(OH)₂D may affect muscle function through both calcium related protein transcription and total body calcium levels. Recently, however, it has transpired that 1,25(OH)₂D also has a transcription-enhancing role on proteins other than those involved directly in calcium metabolism. One such protein, relevant to the discussion of skeletal muscle, is IGFBP-3 working with insulin like growth factor-1 (IGF-1). IGF-1 is a polypeptide, structurally similar to insulin. It induces proliferation, differentiation and hypertrophy of skeletal muscle and is a key component in muscle regeneration. As calcium is a critical modulator of skeletal muscle function, it

follows that vitamin D levels may have a significant impact on muscle function, performance and injury risk. While further research is required to evaluate the level of vitamin D required for optimal muscular function [5, 16, 45, 48].

6.4. Vitamin D and Brain Function

Vitamin D sufficiency is needed to satisfy the vitamin D receptor transcriptional activity in the brain which may be important for brain development as well as for maintenance of mental function in later life [27, 48].

6.5. Vitamin D and Endocrine Function

The vitamin D hormone increases the serum calcium concentrations through different activities. First, it is the only hormone known to induce the proteins involved in active intestinal calcium absorption. Furthermore, it stimulates active intestinal absorption of phosphate. Second, blood calcium concentrations remain in the normal range even when an animal is placed on a no-calcium diet. Therefore, the vitamin D hormone plays an important role in allowing individuals to mobilize calcium from bone when it is absent in the diet. It is very important to note, however, that both vitamin D and parathyroid hormone are required for this mobilization event.

An important aspect of the vitamin D endocrine system is that dietary calcium is favored to support serum calcium concentrations under normal conditions but, when this fails, the system mediates calcium mobilization from bone and reabsorption in the kidney to satisfy the needs of the organism. This results in loss of calcium from the skeleton and can ultimately lead to osteoporosis. Another important aspect is that, except for stimulating mineralization of the skeleton, the vitamin D hormone has not been found to be anabolic on bone by itself [31, 50].

6.6. Vitamin D and Immune Function

Another important area of investigation has been the immune system. Clearly, vitamin D deficiency affects the immune system, especially T cell-mediated immunity, whereas vitamin D in excess actually suppresses certain aspects of the immune system [15, 24]. This has led to investigation of the use of vitamin D compounds to suppress certain autoimmune disorders. The first autoimmune disorder to come under scrutiny is multiple sclerosis, and experimental autoimmune encephalomyelitis has been used as an animal model. This disease can be suppressed or eliminated at any stage of development with adequate amounts of the vitamin D hormone administered orally each day. However, hypercalcemia occurs with this therapy. We now know that the increase in serum calcium concentrations plays some role in this therapeutic response. A clearer example of an autoimmune disease that is regulated by the vitamin D hormone is type 1 diabetes mellitus. Among nonobese diabetic rats, vitamin D deficiency caused a marked increase in incidence and a marked decrease in the lag time required for the initiation of diabetes. Very

important is the fact that large doses of the vitamin D hormone could suppress type 1 diabetes mellitus completely, preventing the destruction of islet cells. Similar results were obtained with models of systemic lupus, inflammatory bowel disease, and rheumatoid arthritis. It is likely that the suppression of these autoimmune diseases involves the vitamin D hormone interacting with T helper lymphocytes, which in turn suppress the inflammatory responses of T helper lymphocytes. Alternative ideas have also been put forth, such as suppression of the dendritic cells that present antigens to the T cells. Although the exact mechanisms of Vitamin D for the regulation of autoimmune diseases are not understood completely, need in depth study [40, 54, 58].

7. Vitamin D and Chronic Diseases

In present years it has been reported that Vitamin D is a key nutrient and plays an important role for the prevention of many chronic diseases, few of those are reported here.

7.1. Cancer

Higher concentrations of 25(OH)D are used by the prostate cells to make 1,25(OH)₂D, which helps keep prostate cell proliferation in check and therefore decreases the risk of prostate cells becoming malignant. Since this observation, it has also been observed that breast, colon, lung, brain, and a wide variety of other cells in the body have the enzymatic machinery to make 1,25(OH)₂D. Thus it has been suggested that raising blood levels of 25(OH)D provides most of the tissues in the body with enough substrate to make 1,25(OH)₂D locally to serve as a sentinel to help control cellular growth and maturation and to decrease the risk of malignancy [1, 2, 17, 18]. This hypothesis has been further supported by the observation that both prospective and retrospective studies revealed that, if the 25(OH)D level is at least 20 ng/mL, decreased risk of developing and dying of colon, prostate, and breast cancers by 30-50 % [26, 30, 32, 42, 43].

7.2. Cardiovascular Diseases

It has been observed that patients with cardiovascular heart disease are more likely to develop heart failure if they are vitamin D deficient. Furthermore, patients with peripheral vascular disease and the common complaint of lower leg discomfort (claudication) were often found to be vitamin D deficient. The muscle weakness and pain was not due to the peripheral vascular disease but because of the vitamin D deficiency. Although the exact mechanism involved in how vitamin D sufficiency protects against cardiovascular heart disease is not fully understood, it is known that 1,25(OH)₂D is one of the most potent hormones for downregulating the blood pressure hormone renin in the kidneys. Furthermore, there is an inflammatory component to atherosclerosis, and vascular smooth muscle cells have a VDR and relax in the presence of 1,25(OH)₂D. Thus, there may be a multitude of mechanisms by which vitamin D is cardioprotective, thus

need further study to reach a specific conclusion [26-28, 37, 57].

7.3. Autoimmune Diseases

Activated T and B lymphocytes, monocytes, and macrophages have a VDR. 1,25(OH)₂D interacts with its VDR in immune cells and has a variety of effects on regulating lymphocyte function, cytokine production, macrophage activity, and monocyte maturation. Thus, 1,25(OH)₂D is considered to be a potent immunomodulator. Vitamin D deficiency is associated with congestive heart failure and blood levels of inflammatory factors, including C-reactive protein and interleukin [26, 44, 47, 54].

7.4. Vitamin D and Other Health Consequences

Studies suggest that vitamin D supplementation reduced risk of developing rheumatoid arthritis, osteoarthritis, and type I diabetes [41, 46]. In another study, vitamin D deficiency increased insulin resistance, decreased insulin production, and was associated with the metabolic syndrome [15, 18, 30, 36]. Vitamin D deficiency has been linked to an increased incidence of schizophrenia and depression [30].

8. Vitamin D and Athletic Performance

Athletic performance is depends on multiple factors including both genetic and environmental influences. Vitamin D is often overlooked element in case of athletic performance. In recent years, it has been proposed that vitamin D plays an important role directly or indirectly in athlete's health, training and performance. It is now recognized that Vitamin D is a unique nutrient for performance development. Vitamin D deficiency is recognized as a worldwide epidemic, athletes are no exception. Several studies have focused a high prevalence of vitamin D insufficiency and deficiency in the general population worldwide, whereas only few studies have found on athletes [30, 52, 53, 59]. Vitamin D deficiency produces muscle fiber atrophy, slow peak muscle contraction; prolonged time to muscle relaxation, and increased risk of chronic musculoskeletal pain associated with different sports persons. It is important to note that type II, fast-twitch muscle fibers are particularly sensitive to the effects of vitamin D deficiency. Type II muscle fibers are extremely important in many of the burst activities necessary for peak athletic performance and fall avoidance. With vitamin D deficiency, atrophy of type II fibers is noted with fatty infiltration and fibrosis. It is observed that the incidence of vitamin D deficiency in elite indoor athletes is up to 94% of basketball players and 83% of gymnasts [36]. However, it is also assumed that participation in outdoor sports provides an advantage for vitamin D production. Seasonal difference in vitamin D status is reported in gymnasts and runners. Sixty-seven percent of participants had levels below 15 ng/mL in winter compared with mean levels of 25 ng/mL in summer [3, 14, 22, 23, 51].

The concept of performance enhancement with sun exposure is not new. It was previously belief and used by Russian and German athletes in 1930s and 1940s [7]. In order to understand how vitamin D may impact on athletic performance, it's important to remember that the active form of vitamin D is not really a vitamin, but rather a steroid in the same way that testosterone is a steroid. It's also a hormone in the same way as growth hormone is a hormone. Activated vitamin D (calcitriol) is a steroid hormone, which regulates more than 1000 vitamin D-responsive human genes, may influence athletic performance [7, 53, 36]. Recent research indicates that these genes affect muscle protein synthesis, muscle strength, muscle size, reaction time, balance, coordination, endurance, inflammation, and immunity—all are important to maintain sports health and athletic performance. An increased vitamin D level in the athletes provides multiple musculoskeletal benefits, increases in muscle protein synthesis, ATP concentration; strength, jump height, jump velocity, jump power, exercise capacity, and physical performance [33, 36, 45, 51]. Vitamin D has a positive effect on overall musculoskeletal function, neuromuscular efficiency and muscle contraction mechanism which directly or indirectly influence the physical performance of the athletes. An appropriate vitamin D level prevents injury and fall, foster better recovery, increased muscle relaxation and improves muscle pain and weaknesses.

9. Conclusion

Evidence suggests that adequate amount of vitamin D is essential for the betterment of health in general and the prevention of many chronic diseases. Athletes may have a positive effect to improve their optimal performance. It is proposed that Vitamin D is a potent nutrient and working as a regulator of several physiological functions in the human body. Some of these functions are well recognized but many are yet to be researched to understand the complete mechanism of action as it plays in the human body. Hope this review study will unfold some fundamental concept of vitamin D and how it is biologically important for the maintenance of optimal health and reach peak athletic performance.

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