

Meta-Analysis Describing Relationship of Fatigue in Elderly with Hypovitaminosis

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Abstract

Fatigue is the common complaint by the elderly individuals. There are several indications associated with fatigue. However, the hallmark is the state of tiredness or "low energy" due to nutritional deficiencies mainly vitamins. Among several others, Vitamin D is crucial in maintaining elderly health due to its association with the several vital processes like strengthening of the immune functions, cardio protective and supporting bones strength besides cognitive functioning. Vitamin D is also required for metabolic processes in the liver and support kidney functionality. A deficiency of vitamin D among elderly individual is linked with fatigue syndrome. The research uses a meta-analysis approach to gather, refine and scrutinize data associating old people fatigue with Vitamin D hypovitaminosis. The ultimate objective is to generate data from the authentic sources in order to facilitate further data assessment and analyses. Although hypovitaminosis is prevalent among infants and elderly also, however, this study centers its investigation on seniors. The research explores this group because it is the most affected by hypovitaminosis D. Deficiency of Vitamin D is considered as increasingly important for understanding fracture risk, due to malabsorption of calcium and phosphorus required for bones strengthening. The data generated from this meta-analysis highlight the widespread prevalence of hypovitaminosis D among those with long-term illnesses particularly elderly individuals that need appropriate clinical managements.

Keywords: Fatigue; Vitamin D; Hypovitaminosis; Calcium Deficiency; Elderly Individuals

Introduction

Elderly individuals are prone to several nutritional deficiencies. Among these vitamins and minerals deficiencies have significant implications on their health. As the people age, their caloric intake decline and so is the necessary nutrients. As such it is considered neces-

sary to have adequate nutritional requirements for the older people, and they should have a healthy diet with appropriate caloric and nutritional elements. The other relevant issue is that aging is associated with a decline in the physiological functioning of various organs and particularly the efficiency of the human body in absorbing essential vitamins and nutrients also decline. This has emerged as a challenge for the healthcare of ever increasing aging population. The nutritional deficiencies among older people lead to several ailments and weakened their human body, particularly fatigue among elderly individuals is considered mainly due to the nutritional deficiencies like Vitamin D and several others.

The dietary requirements are also linked with the environment, and one glaring example is the Vitamin D. Human body is unable to fulfill its necessary needs from the diet, and in partial Vitamin D requirement is fulfilled through its synthesis in the skin when sunlight hit the body. As such in describing vitamin D hypovitaminosis it is important to have a clear understanding about this vitamin that is also called as sunshine vitamin [1]. In human Vitamin D is comprised of two forms D2 and D3. The D3 component of the Vitamin D is considered as the natural one and is synthesized when human skin is exposed to the Ultraviolet B, a component of the sunlight [2,3]. The D2 component of the Vitamin D is not synthesized within the human body and is provided externally through various foods. In the liver and kidney, both D2 and D3 are further metabolized forming biologically active Vitamin D that mainly is involved in calcium and phosphorus absorption. As such deficiency of Vitamin D is also manifested in the form of lowered amounts of both these essential elements in the human body [4]. A recent clinical study suggests that among the two vitamin D3 is more effective in maintaining required serum levels of this essential nutrient to support necessary physiological functionality. In concluding its findings, this study quotes that "With the use of a daily dose of vitamin D relevant to public health recommendations (15 ug) and in vehicles relevant to food-fortification strategies, vitamin D3 was more effective than vitamin D2 in increasing serum 25(OH)D in the wintertime. Vitamin D3 may, therefore, be a preferred form to optimize vitamin D status within the general population [5]". Notably, in several parts of the world the sunshine decline in winter and as such body should be provided more vitamin D for its required physiological functioning.

The fatigue syndrome among elderly has several other underlying causes. However, it is becoming more important to understand this loss of energy and vigor among the elderly that caused several other complications also. Aged, individuals synthesize relatively lesser levels of vitamin D3 for their decreased outside activities for being not too much exposed to the sunlight required for synthesis of this essential nutrients. This meta-analysis evaluated fatigue linkage with hypovitaminosis D and data generated suggest; it is essential to consider supplementing the elderly diet with the required amount of vitamin for maintaining their good health and avoiding fatigue mainly linked with hypovitaminosis D.

Background of the Study

Hypovitaminosis D is prevalent among older people, and so is the case in some adults, one of the leading causes of their higher fatigue levels [6,7]. Higher prevalence of hypovitaminosis D linked fatigue among elderly is their relatively lesser exposure to the sunshine. Besides fatigue, hypovitaminosis D is also a primary cause of body aches and pains among the elderly people also. A study by Farouk., *et al.* (2016) explored the association of hypovitaminosis D amongst patients who are admitted for hip fracture [8]. These patients often have less energy to do everyday tasks and due to an imbalance in their posture are prone to falls that lead to fractures and other injuries. According to previous researchers, most patients suffering from hypovitaminosis D are suffering from other long-term illnesses, such as cancer, diabetes, obesity and even depression. The majority of patients with musculoskeletal pain, headache and fatigue suffer some sought of hypovitaminosis and among this hypovitaminosis D is relatively higher [9,10]. It is important to mention here that fatigue equally affects both elderly men and women.

There are some key factors which make elderly people more susceptible to fatigue as a result of hypovitaminosis.

- 25 dihydroxy Vitamin D is an active form of Vitamin D for hormones
- Hypovitaminosis D is defined as the level of 25 (OH)D < 30 nmol/L (< 12 ng/mL)

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- 25 hydroxyvitamin D 25(OH)D) for the main reservoir and vitamin in our bodies
- An elderly person above 70 years synthesizes less than 30% Vitamin D as compared to the young who are exposed to the sun

The major health benefits of vitamin D are summarized as below:

- Vitamin D plays a crucial role in muscular function.
- Hypovitaminosis D is more prevalent in postmenopausal women and increases with age.
- Replacement of Vitamin D takes place within the body to improve muscle function, which reduces the risk of different factors associated with hypovitaminosis D.
- Vitamin D plays a crucial role in calcium for phosphorus homeostasis.
- The symptoms of hypovitaminosis D are similar to that for muscle fatigue and low bone mineral density.

Vitamin D plays a central role in phosphorus and calcium homeostatic processes. The natural form of Vitamin D is ergocalciferol found in several food items, and this supports the synthesis taking place beneath the skin, which is triggered by exposure to ultraviolet light. Such a form of Vitamin D has to change with 25-hydroxyvitamin D (25(OH))D, which facilitates hydroxylation in the kidney. The active function of hormones in the body enables perfect interaction with the Vitamin D receptor (D), which is based on dependent proteins. The biological effects may play some part in calcium and phosphorous homeostatic processes.

Hypovitaminosis D or Vitamin D insufficiency is reflected in the form of its lowered levels in the serum. Hypovitaminosis D is generally defined as serum levels of 25 (OH) D below 30 ng/mL. Hypovitaminosis D causes the depletion of muscle function which increases the risk of falls among elderly.

Apparently, Vitamin D plays a significant role in the metabolism of calcium and phosphorus in humans. However, with the depletion of bodily systems, especially the digestive, renewal and skeletal systems, the metabolism is impaired, hence resulting in fatigue. The Vitamin D endocrine functions play a central role in skeletal and homeostatic integrity in the development and integrity of several tissues like bone formation. The 25(OH)D originates from a substance within a group of secosteroids called Vitamin D2 that occur naturally and facilitate self-synthesis in the skin generating Vitamin D3 synthesis takes place in the skin is triggered by ultraviolet light B to produce Vitamin D3.

Objectives and Justification of the Study

The prevalence of fatigue mainly associated with deficiency of vitamin D is widespread among elderly individuals. The fatigue syndrome due to hypovitaminosis D is also strongly linked to inflammatory conditions among elderly people also [11]. Besides hypovitaminosis, both the communicable and non-communicable diseases such as chronic obstructive pulmonary diseases (COPD), human immunodeficiency virus (HIV) infections and cancers also lead to severe fatigue suggesting that the etiology of fatigue varies among people [12,13]. The overall pathological aspects of fatigue are associated with the generation of free radicals that induce oxidative stress [14,15]. For elderly people, the experience of fatigue is naturally comparable to that of a patient with chronic fatigue syndrome. There are several factors linked with fatigue syndromes among elderly individual. The majority of these are as a result of reduced physical activity as well several emotional health issues. Hence, the objectives of this study are to evaluate the relationship between hypovitaminosis D and fatigue among elderly individuals. Major avenues to be explored are:

- 1. Explore the occurrence of fatigue in elderly hypovitaminosis D sufferers.
- 2. Determine the relationship between inflammatory diseases and their influence on the development of hypovitaminosis D.
- 3. Establish the age variable and its relevance for understanding the occurrence of hypovitaminosis D.
- 4. Find evidence to support the hypothesis that fatigue is generally a result of the presence of hypovitaminosis D.

Materials and Methods

Literature Review

It has been estimated that at least one billion people could be suffering from vitamin D hypovitaminosis globally [16]. As vitamin D is mainly synthesized by the human body under the influence of the sunshine and people having less exposure to the sun like elderly individuals relatively suffers more than the adults having enough sunlight exposures. Furthermore, seniors mainly suffer from long-term illnesses such as cancer and diabetes over extended periods of time and are known to be suffering from some sort of deficiency of vitamin D also linked with decreased levels of calcium and parathyroid hormone [17,18]. Furthermore, vitamin D deficiency indirectly impairs absorption of phosphorus and calcium thus leading to several ailments. The Brock., *et al.* (2013) study provides a deeper assessment of the impact of fatigue and its association with nutritional deficiencies affecting elderly women [19]. This study alludes that hepatic and kidney failure associated with the hypovitaminosis D.

The Plotnikoff (2003) study indicates that the high prevalence of hypovitaminosis D in elderly populations can be explained by the type of hypovitaminosis and varies slightly based on sex and age [20]. Along with similar lines Williams., *et al.* explored known determinants of Vitamin D status to allow for a better assessment of the presence of Vitamin D among East Asian immigrants [21]. Vitamin D levels naturally depend on sunlight exposure [16]. A study explored the interrelationship of diabetes and the development of Vitamin D complications, noting the utility of insulin enhancers [22]. The findings of this particular study link hypovitaminosis D with cardiovascular risks. However, researchers exploring fatigue levels have failed to understand the essence of the hypovitaminosis D myopathy (HDM), which is misdiagnosed among older, hospitalized adults who are affected by hypovitaminosis D [23].

Khawaja., et al. (2017) study describes the high prevalence of fatigue among people is due to a fundamental loss of functionality and suggest "Cholecalciferol 50,000 IU bi-monthly is required to maintain sufficient 25(OH)D levels" among Jordanian individuals suffering from hypovitaminosis D [24]. This study further elaborates on vitamin D deficiencies symptoms observed in patients suffering osteomalacic bone disease. Biopsies have also shown that, among patients presenting such symptoms, the disease is clinically detectable in 96.7% of cases. Hypovitaminosis D is naturally often misdiagnosed given the wrong understanding of the gradual process that enables its development. A major factor in misdiagnosis is the non-specificity of different symptoms such as muscle pain, parenthesis, and bone pain. An interesting study has defined the deficiency of vitamin D association with vitamin D receptor (VDR) "Vitamin D deficiency is associated with the increase of circulating cholesterol in the people of northern China by enhancing hepatic cholesterol biosynthesis, which was linked to the reduction of transcriptional activity of VDR" [25]. Other researchers have explored the classical functions of bone metabolic regulation based on Vitamin D presence in multiple biological targets for mediated hormone receptors. Research suggests that the central nervous system depends on the entrance of Vitamin D in cerebrospinal fluid that involves the crossing of the blood- brain barrier. This barrier protects the central nervous system, and it has been reported that vitamin D plays a major role in the integrity of BBB thus suggesting its role in protecting the human central nervous system [26,27]. The CSF vitamin D levels naturally correlate with the serum for various physiological conditions including cognitive function [28]. As far as Vitamin D mediated neuroprotection is concerned different roles need vitamin D. Rodriquez., et al. (2014) further elaborates that the binding of Vitamin D and the VDR naturally triggers a neuronal protection in various degenerative processes, which includes anti-inflammatory actions and various anti-oxidations [29]. The serum levels balance the regulation of Vitamin D that is involved in the regulation of the gene expression for numerous neurotransmitters of the brain involving serotonin and dopamine effects. Roy., et al. (2014) also observed and the neurosteroid properties of Vitamin D encourage the normalization of Vitamin D status, which is involved in addressing the decline of cognitive abilities and other brain functionalities [30].

Most importantly, cross-sectional studies evaluated in this meta-analysis on Vitamin D have provided possible epidemiological evidence of an association between the presence of hypovitaminosis and increased incidence of dementia. Mostly, the relationship between Vitamin D and dementia is unveiled and explained for different stages of the disease. The prodromal stages of the primary neurocognitive disorders involve impaired cognitive functionality (Table 2). Hence, one cannot understand the relationship between fatigue and hypovitaminosis D as linear as Vitamin D levels are associated with cognitive performance [31,32].

The results give vitamin D thresholds that provide clinical value in understanding cognition levels. The high prevalence of hypovitaminosis D in elderly people can, therefore, be explained by a variance of between 10 and 30 ng/mL. Deficiencies in the primary care setting are scarce and used for the different prevalence rates and various potential associations and clinical symptoms such as body index, Vitamin D, and age. According to Merlo., *et al.* (2015) levels of 25 hydroxycholecalciferol (25(OH) D) is linked with several diseases in primary care settings [33]. Essentially, musculoskeletal pain, age, and fatigue are indications that Vitamin D levels are higher than 60.6 +/- 22.2 nmol, which was targeted at the 75 nmol level. Mostly, close to 60% of patients in such primary care are reported to have a central weakness in their body mass index that is associated with lowered 25 (OH) D levels.

Apparently, from a collective point of view, researchers believe that elderly people suffer from low bone density due to increased risk of osteoporosis and fractures linked with hypovitaminosis D. The 25-hydroxy Vitamin D levels can be found in a large proportion of patients with some stress fracture. The prospective, non-randomized therapeutic study of Vitamin D and fatigue points to high fatigue levels and unstable health. Sherman., *et al.* (2014) argue that a standard methodology of determining fatigue in a cancer patient is a shift in Vitamin D supply. Stabilizing Vitamin D levels improves their fatigue levels, which is better medical approach because it can help to respond to possible chronic conditions [34] effectively.

Methodology

This study utilized a meta-analysis approach that allows for proper investigation through cross-sectional studies which incorporate systematic reviews and concepts based on different baseline information. The analysis is based on searches conducted in the primary medical databases, including PubMed, that provides free access to the MEDLINE and the National Library of Medicine (NLM) database including citations and abstract of studies in the field of medical, nursing, dental, veterinary, health care, and preclinical sciences journal articles [34]. Most of the research listed has some sought of similarity and is aligned with possible search criteria that involved looking for articles that have similar information for hypovitaminosis D. Given that many journals use similar wording in titles, it is hard to have some sought of predefined search criteria. However, the data variables were aligned, and the integral focus was on primary research, especially on articles that contained a sound scientific abstract associated with hypovitaminosis D among elderly individuals.

Meta-analysis was conducted by combining the results of the different studies used to address a set of related research hypotheses, enabling data mining for hypovitaminosis D (Table 1 and 2). The goal of the meta-analysis was to allow the assertion of data, which will be useful for the selection process for this particular topic. However, given the nature of this research, we will not be applying the data in a complex way but describe various statistical and analytical tools that draw on the utility of different methodologies and are aligned with the purpose of this research i.e. hypovitaminosis D among elderly individuals. A table generated (Table 2) through our evaluation describes the findings.

Researcher	Year	Sample	Prevalence Cases
(Farouk., <i>et al</i> . 148 - 152)	2016	133	60%
(Khawaja., <i>et al</i> . 172 - 179)	2017	71	69%
(Pittas., <i>et al</i> . 70 - 78)	2010	Nil	Nil
(Stoker., et al. 231 - 236)	2013	384	58%
(Williams., et al.)	2017	211	55%

Table 1: List of Studies Included in the Current Meta-Analysis and Sample Size.

Author – Study Year		Salient Feature of the Study	Strengths and Limitations of the Study	Policy Implications Towards Elderly Health care
Farouk., <i>et al.</i> 2016 [8]	• • •	The study explored 133 patients with hip fracture Patients' median age was 70 years. 51.9% were females Patients were diagnosed with BMD and high BMI. Lack of abundant sunshine leads to hypovitaminosis D	The article is appropriate because it in- corporates primary research in proving the relationship between hypovitamino- sis D and the development of fatigue. The research is only centered on females, hence not actually balancing the concept of gender.	The research is relevant because it has several practical implications. For instance, it uses primary research on females with a median age of 70 years. This shows that elderly people are the most affected by the problem of rela- tionship fatigue.
Khawaja., <i>et al.</i> 2017 [24]	•	The article made weekly and daily comparisons for patients with hypovitaminosis D 71 patients with hypovitaminosis D were involved in the study. Participants were assigned 2-dose regimens for cholecalciferol A negative correlation was found between serum 25-hydroxy vitamin D for BMI	The research conducts primary research on 71 patients. It finds a negative corre- lation with between serum 25 (OH). The research does not, however, investigate the relationship between fatigue and hy- povitaminosis D.	The research has some policy implica- tions pointing to the introduction of a cholecalciferol regimen and examines BMI.
Pittas. <i>, et al</i> . 2010 [38]	•	 Calcium and phosphorus promote bone mineralization reducing risk of hypovitaminosis D Screening is necessary for reducing the plasma with total 25 hydroxyvitamin D. The routine part requires possible parental and enteral nutrition The restoration of optimal Vitamin D is done by way of a supplemental vitamin D that is needed for the sunlight in ultraviolet B radiation 	The research is appropriate because it goes an extra mile in showing the useful- ness of calcium and phosphorous in creat- ing a strong Vitamin D body. The journal also focuses on the importance of nutri- tion in promoting a stable and working health pattern. However, there are limits because the journal does not relate Vita- min D to fatigue	The research points to hydroxyvita- min D and its importance to enteral nutrition. The research pushes policy development on the restoration of Vi- tamin D.
Stoker. <i>, et al</i> . 2013 [45]	•	Vitamin D has been linked to hip and knee osteoarthritis. The study focused on adult patients who had undergone spine surgery that was involved in cer- vical magnetic resonance imaging (MRI) The study compared at least 384 non-deficient patients and 162 Vitamin D-deficient. It was agreed that vitamin deficiency was associated with cervical disk herniation	The publication shows the close relation- ship between hip and multiple fatigues. The study conducted primary research on 384 patients. Such patients are naturally confined to the house, hence lacking suf- ficient sunlight. The study, however, in- volved magnetic resonance imaging. This can be a major problem because it can also cause fatigue.	The research moves towards intro- ducing magnetic resonance imaging (MRI). The study, in particular, fo- cused on cervical disk herniation.
Williams., et al. 2017 [21]	•	Reviewed conflicting data concerning the relationship between Vitamin D and fatigue Vitamin D is associated with sustained low-energy for fractures and compared with ankle sprains and osseous involvement Screening for hypovitaminosis D for plasma total of 25-hydroxyvitamin D as a routine patient requirement	The study examines data surrounding the relationship between Vitamin D and as- pects of fatigue. However, the study does not conduct a primary research. In fact, it explains the screening of hypovitaminosis D for patient requirements	The research influences policy devel- opment by showing the importance of screening for hypovitaminosis as routine part of patient requirements.

Table 2: Descriptive Analysis of Studies Evaluated for Describing Vitamin D Hypovitaminosis with Fatigue among Elderly Individuals.

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Results and Discussion

The data generated from our evaluations are summarized in Table 2. A total of five studies met our criteria that we evaluated extensively. A comparative analysis of these studies suggests hypovitaminosis D impact on elderly individuals' health. As evidenced from the meta-analysis, Vitamin D hypovitaminosis is a significant issue as far as elderly people are concerned. The relative mobility of older adults is limited, and they have to stay inside just getting minimal sunlight that contributes towards Vitamin D hypovitaminosis [35]. Exposure to sunlight is considered essential as far as Vitamin D metabolic aspects within the human body are concerned and the biochemical mechanisms described in the introduction section [36,37]. In general, it is considered that almost 50% of the World population is subjected to Vitamin D associated hypovitaminosis. However, the severity level gets more pronounced among elderly who are relatively less mobile and get minimal sunshine necessary for the synthesis of natural Vitamin D within the human body [16]. Based on these observations, it is entirely plausible to presume that Vitamin D deficiency is an epidemic, particularly among people having lesser sunlight and the one living in regions having lower sunshine. Vitamin D supplementation is usually recommended for inhabitants in the area having less sun, and mainly the number of sunlight exposure decreases among people residing in these regions. Although deficiency of Vitamin D into the human body can be reduced through external supplementation, however, the naturally synthesized component is considered more beneficial and easy to get metabolized. In this meta-analysis, the Khawaja., et al. study explored Vitamin D dosage strategies amongst Jordanians population suffering from Vitamin D hypovitaminosis [24]. A problem observed was the balanced levels of Vitamin D intermediary metabolites mainly the maintaining required levels of 25(OH)D. Apparently, determining how much Vitamin D needed depends on a variety of factors, hence inducement is not always appropriate. It requires multiple testing to determine ideals level and develop appropriate guidelines. However, the serum levels of Vitamin D is considered as the primary reliable biomarker.

All research that was evaluated in this meta-analysis had a consensus that manifestation of fatigue among elderly patients is a result of severe hypovitaminosis D, which also lead to general skeletal pain. Knusten., *et al.* indicate that Vitamin D hypovitaminosis is very often misdiagnosed as chronic fatigue syndrome and depression [11]. Hence, the clinical implications of Vitamin D hypovitaminosis are highly significant particularly for the health care aspects of elderly people. Some studies suggest supplementation with Vitamin D as essential for managing elderly individuals health conditions mainly involving disease relevant to calcium and phosphorus requirements and several others [38]. This becomes more meaningful for the regions having relatively lesser sunlight where Vitamin D deficiency among elderly is manifested in the form of osteomalacia and several other ailments. During such stages, it sounds that calcium intake is almost zero. However, the underlying cause is lowered level of Vitamin D required for calcium absorption. Such a patient experiences no healing and a prolonged stay in hospital as well as pancreatic carcinoma. Based on the different experimental models, it has been found Vitamin D deficiency inhibits insulin secretions associated with the beta-cell functionality of hypovitaminosis D [39,40]. Among several others, Vitamin D deficiency induced oxidative stress is considered as the prominent factor in reducing insulin synthesis. The oxidative stress is linked with damage to bodily tissues.

It has also been suggested that Vitamin D hypovitaminosis D is a potential risk factor for multiple sclerosis [41,42]. Hypovitaminosis D as witnessed in older individuals may induce postural deformities among older individuals [43,44]. The human requirements for Vitamin D are such that the latter plays an important immunological role. Hypovitaminosis D 25 (OHD) and PTH for secondary hyperparathyroidism (SHPT) can lead to Vitamin D insufficiency which creates conditions associated with osteoporotic or osteomalacic bone changes. There are consequences for calcium status as well as bone fragility and fracture, which might influence osteoporosis fracture risk.

A study by Stoker., *et al.* (2013) provides a robust assessment of hypovitaminosis D and cervical disk herniation [45]. This article further sheds light on how Vitamin D deficiency is associated with increased serum alkaline and phosphatase as well as parathyroid hormone PTH levels that result in an imbalance in certain necessary elemental turnover.

Limitations of the study

Major limitations of this study are that our conclusions are based on data generated from other laboratories with a strong presumption of the validity of data. Furthermore, Vitamin D deficiency is an active area of research, and a plethora of literature exists related it lack

of Vitamin D and its impact on infants and juvenile health conditions [46-48]. However, the association of Vitamin D deficiency linkage with fatigue among elderly individuals is unique in nature and warrants further studies.

Conclusions and Recommendations

The prevalent data reaffirms the previous findings that lack of energy due to Vitamin D deficiency is correlated with the risks elderly individuals face. Lesser energy levels associated with fatigue are considered as the major factor contributing towards uncontrolled body movements and mainly falls leading to fractures and injuries. Several clinical trials have reaffirmed Vitamin D hypovitaminosis suggesting clinical management of serum Vitamin D levels among elderly population and a regular checkup [19,49-51]. Data emerging from the current meta-analysis clearly suggest a close relationship between fatigue in older persons and Vitamin D hypovitaminosis. A critical evaluation of current studies further elaborates on hypovitaminosis defining an association between the supplies of calcium and phosphorous. The existing literature provides a well-detailed account of the human subjects, suffering from Vitamin D hypovitaminosis. The research adopted a meta-analysis strategy, as a way to analyze, scrutinize and evaluate the opinions of other researchers. The research, therefore, suggests that elderly people are more prone to fatigue because they are more likely to suffer from Vitamin D hypovitaminosis.

It is also important to keep in mind that between the two D2 and D3 which form of vitamin should be supplemented in nutrition. This issue has been discussed by several studies. However, a recent clinical trial conclusively suggests vitamin D3 is the better option for individuals of all ages. As such, based on the information generated from our meta-analysis and existing studies future efforts should be directed towards monitoring levels of vitamin D (D2 and D3) among elderly and in case the levels are lowered, efforts should be to stabilize its serum levels that can ultimately improve the quality of life among elderly individuals.

Bibliography

- 1. Muscogiuri G. "New light on an old vitamin: The role of the sunshine vitamin D in chronic disease". *Reviews in Endocrine and Metabolic Disorders* 18.2 (2017): 145-147.
- Hart PH and S Gorman. "Exposure to UV Wavelengths in Sunlight Suppresses Immunity. To What Extent is UV-induced Vitamin D3 the Mediator Responsible?" *Clinical Biochemist Reviews* 34.1 (2013): 3-13.
- Webb AR and MF Holick. "The role of sunlight in the cutaneous production of vitamin D3". Annual Review of Nutrition 8 (1988): 375-399.
- 4. Grundmann SM., *et al.* "The High Calcium, High Phosphorus Rescue Diet Is Not Suitable to Prevent Secondary Hyperparathyroidism in Vitamin D Receptor Deficient Mice". *Frontiers in Physiology* 8 (2017): 212.
- Tripkovic L., *et al.* "Daily supplementation with 15 mug vitamin D2 compared with vitamin D3 to increase wintertime 25-hydroxyvitamin D status in healthy South Asian and white European women: a 12-wk randomized, placebo-controlled food-fortification trial". *American Journal of Clinical Nutrition* (2017).
- Coombes JS., et al. "Effects of vitamin E deficiency on fatigue and muscle contractile properties". European Journal of Applied Physiology 87.3 (2002): 272-277.
- 7. Mokta J., et al. "Vitamin D Deficiency Presenting as Fatigue". Journal of the Association of Physicians of India 64.8 (2016): 105.
- 8. Farouk O., *et al.* "Hypovitaminosis D Among Patients Admitted With Hip Fracture to a Level-1 Trauma Center in the Sunny Upper Egypt: Prevalence and Associated Correlates". *Geriatric Orthopaedic Surgery and Rehabilitation* 7.3 (2016): 148-152.

- 9. Arnall FA., *et al.* "Between-days reliability of electromyographic measures of paraspinal muscle fatigue at 40, 50 and 60% levels of maximal voluntary contractile force". *Clinical Rehabilitation* 16.7 (2002): 761-771.
- 10. Walsh JA., et al. "Work productivity loss and fatigue in psoriatic arthritis". Journal of Rheumatology 41.8 (2014): 1670-1674.
- 11. Knutsen KV., *et al.* "Vitamin D status in patients with musculoskeletal pain, fatigue and headache: a cross-sectional descriptive study in a multi-ethnic general practice in Norway". *Scandinavian Journal of Primary Health Care* 28.3 (2010): 166-171.
- 12. Sharpe M., *et al.* "Follow up of patients presenting with fatigue to an infectious diseases clinic". *British Medical Journal* 305.6846 (1992): 147-152.
- 13. Franssen PM., *et al.* "The association between chronic diseases and fatigue in the working population". *Journal of Psychosomatic Research* 54.4 (2003): 339-344.
- 14. Barclay JK and M Hansel. "Free radicals may contribute to oxidative skeletal muscle fatigue". *Canadian Journal of Physiology and Pharmacology* 69.2 (1991): 279-284.
- 15. Richards RS., et al. "Free radicals in chronic fatigue syndrome: cause or effect?" Redox Report 5.2-3 (2000): 146-147.
- 16. Nair R and A Maseeh. "Vitamin D: The "sunshine" vitamin". Journal of Pharmacology and Pharmacotherapeutics 3.2 (2012): 118-126.
- 17. Berridge MJ. "Vitamin D deficiency and diabetes". Biochemical Journal 474.8 (2017): 1321-1332.
- 18. Ma K., *et al.* "Vitamin D deficiency is associated with a poor prognosis in advanced non-small cell lung cancer patients treated with platinum-based first-line chemotherapy". *Cancer Biomark* 18.3 (2017): 297-303.
- 19. Brock KE., *et al.* "Vitamin D status is associated with sun exposure, vitamin D and calcium intake, acculturation and attitudes in immigrant East Asian women living in Sydney". *Journal of Steroid Biochemistry and Molecular Biology* 136 (2013): 214-217.
- Plotnikoff GA and JM Quigley. "Prevalence of severe hypovitaminosis D in patients with persistent, nonspecific musculoskeletal pain". Mayo Clinic Proceedings 78.12 (2003): 1463-1470.
- 21. Williams BR., et al. "Vitamin D Levels Do Not Predict Risk of Metatarsal Fractures". Foot and Ankle Specialist (2017).
- 22. Boucher BJ. "Vitamin D insufficiency and diabetes risks". Current Drug Targets 12.1 (2011): 61-87.
- 23. Fabbriciani G., *et al.* "Diffuse muscoskeletal pain and proximal myopathy: do not forget hypovitaminosis D". *Journal of Clinical Rheumatology* 16.1 (2010): 34-37.
- 24. Khawaja N., *et al.* "Vitamin D Dosing Strategies Among Jordanians With Hypovitaminosis D". *Journal of Pharmacy Practice* 30.2 (2017): 172-179.
- Li S., et al. "Increase of circulating cholesterol in vitamin D deficiency is linked to reduced vitamin D receptor activity via the Insig-2/ SREBP-2 pathway". Molecular Nutrition and Food Research 60.4 (2016): 798-809.
- 26. Enkhjargal B., et al. "Intranasal administration of vitamin D attenuates blood-brain barrier disruption through endogenous upregulation of osteopontin and activation of CD44/P-gp glycosylation signaling after subarachnoid hemorrhage in rats". Journal of Cerebral Blood Flow and Metabolism 37.7 (2017): 2555-2566.

- 27. Won S., *et al.* "Vitamin D prevents hypoxia/reoxygenation-induced blood-brain barrier disruption via vitamin D receptor-mediated NF-kB signaling pathways". *PLoS One* 10.3 (2015): e0122821.
- 28. Hooshmand B., *et al.* "Vitamin D in relation to cognitive impairment, cerebrospinal fluid biomarkers, and brain volumes". *Journals of Gerontology Series A Biological Sciences and Medical Sciences* 69.9 (2014): 1132-1138.
- 29. Rodriguez CE and A Pessier. "Pathologic changes associated with suspected hypovitaminosis A in amphibians under managed care". *Zoo Biology* 33.6 (2014): 508-515.
- 30. Roy S., *et al.* "Correction of Low Vitamin D Improves Fatigue: Effect of Correction of Low Vitamin D in Fatigue Study (EViDiF Study)". *North American Journal of Medical Sciences* 6.8 (2014): 396-402.
- 31. Annweiler C., *et al.* "Vitamin D and cognitive performance in adults: a systematic review". *European Journal of Neurology* 16.10 (2009): 1083-1089.
- 32. Wilkins CH., *et al.* "Vitamin D deficiency is associated with worse cognitive performance and lower bone density in older African Americans". *Journal of the National Medical Association* 101.4 (2009): 349-354.
- Merlo C., et al. "Vitamin D Deficiency in Unselected Patients from Swiss Primary Care: A Cross-Sectional Study in Two Seasons". PLoS One 10.9 (2015): e0138613.
- 34. Yoo S and J Choi. "On the query reformulation technique for effective MEDLINE document retrieval". *Journal of Biomedical Informatics* 43.5 (2010): 686-693.
- 35. Hodkinson HM., et al. "Sunlight, vitamin D, and osteomalacia in the elderly". Lancet 1.7809 (1973): 910-912.
- 36. Gloth FM., *et al.* "Vitamin D deficiency in homebound elderly persons". *Journal of the American Medical Association* 274.21 (1995): 1683-1686.
- 37. Whitmore SE. "Vitamin D deficiency in homebound elderly persons". *Journal of the American Medical Association* 275.11 (1996): 838-839.
- 38. Pittas AG., *et al.* "Role of vitamin D in adults requiring nutrition support". *Journal of Parenteral and Enteral Nutrition* 34.1 (2010): 70-78.
- 39. Erol M., *et al.* "Vitamin D deficiency and insulin resistance as risk factors for dyslipidemia in obese children". *Archivos Argentinos De Pediatria* 115.2 (2017): 133-139.
- 40. Tao S., et al. "Vitamin D deficiency causes insulin resistance by provoking oxidative stress in hepatocytes". Oncotarget (2017).
- 41. DeLuca HF and L Plum. "UVB radiation, vitamin D and multiple sclerosis". *Photochemical and Photobiological Sciences* 16.3 (2017): 411-415.
- 42. Pierrot-Deseilligny C and JC Souberbielle. "Vitamin D and multiple sclerosis: An update". *Multiple Sclerosis and Related Disorders* 14 (2017): 35-45.
- 43. Boersma D., *et al.* "Vitamin D status in relation to postural stability in the elderly". *Journal of Nutrition Health and Aging* 16.3 (2012): 270-275.

- 44. Krause M., *et al.* "Vitamin D deficiency intensifies deterioration of risk factors, such as male sex and absence of vision, leading to increased postural body sway". *Gait Posture* 39.1 (2014): 166-171.
- 45. Stoker GE., *et al.* "Hypovitaminosis D and Cervical Disk Herniation among Adults Undergoing Spine Surgery". *Global Spine Journal* 3.4 (2013): 231-236.
- 46. Cetinkaya M., *et al.* "Maternal/neonatal vitamin D deficiency: a new risk factor for necrotizing enterocolitis in preterm infants?" *Journal of Perinatology* 37.6 (2017): 673-678.
- 47. Puthuraya S., *et al.* "Does vitamin D deficiency affect placental inflammation or infections among very low birth weight infants?" *Journal of Maternal-Fetal and Neonatal Medicine* (2017): 1-7.
- 48. Sudfeld CR., *et al.* "Vitamin D Deficiency is not Associated with Growth or the Incidence of Common Morbidities Among Tanzanian Infants". *Journal of Pediatric Gastroenterology and Nutrition* (2017).
- 49. Bentes CM., *et al.* "Association between muscle function and body composition, vitamin D status, and blood glucose in postmenopausal women with type 2 diabetes". *Diabetes and Metabolic Syndrome* (2017).
- 50. Brannstrom A., *et al.* "Vitamin D in relation to bone health and muscle function in young female soccer players". *European Journal of Sport Science* 17.2 (2017): 249-256.
- 51. Dawson-Hughes B. "Vitamin D and muscle function". Journal of Steroid Biochemistry and Molecular Biology (2017).

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