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Potential Role of Vitamin D in Management of Depression and Anxiety

Hadiqa Shahzadi[1], Dr. Safeena Amjad[1], Laiba Abdullah[3]

1. *Department of Nutrition & Health Promotion, University of Home Economics, Lahore.*
2. *Department of Computer Science, UET, Lahore, Pakistan*

Corresponding Author:

Sawera Butt
sawerabutt891@gmail.com

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ABSTRACT

The problem of depression and anxiety is found in people across all populations, and, to a large extent, this may be due to the deficiency in vitamin D, which has also been linked with schizophrenia and seasonal affective disorder. Vitamin D or cholecalciferol is a fat-soluble vitamin, indispensable for cell growth, neuromuscular and immune function, and balance of calcium and phosphorus in the body. From existing literature, this paper will address the effects of vitamin D on symptoms of anxiety and depression. We analyzed studies measuring serum vitamin D levels in patients with depression as compared to non-depressed controls. Our analysis demonstrated that de- pressed cases significantly expressed lower levels of vitamin D as compared to non-depressed controls. Moreover, those with the lowest levels of vitamin D expressed a higher risk for depression and anxiety. Supplementation with vitamin D has significantly reduced the symptoms of anxiety and depression. The results of our study imply that vitamin D is involved in mental health, enables antioxidant properties that enhance the functioning of brain tissues, and can be involved in mood disorders' prevention. Accordingly, these findings indeed reflect the importance of adequate vitamin D levels in mental well-being and highlight the need for additional research to assess the therapeutic potential of vitamin D in managing depression and anxiety.

Keywords:

Vitamin D, Depression, Anxiety, Schizophrenia, Cholecalciferol, MDD, Antioxidant, Supplementation

1. Introduction

Vitamin D is paramount to the operation of the body and the overall condition of the individual, and minute quantities suffice. This is because it functions to help the body absorb calcium and phosphorus, minerals that are essential for the growth and repair of bones in a healthy manner. Being fat- soluble means that it is dissolvable in fats and oils, and they therefore serve as solvents for the vitamin. Among the foods it is found in include fish oil, egg yolks, and dairy products (Nair et al., 2012).

Vitamin D3 is a hormone synthesized endogenously by the human body and is also a crucial dietary constituent that plays a vital role in maintaining optimal bone, tooth, and muscle health. While vitamin D3 can be sourced from a

limited range of foods, solar radiation exposure remains the most optimal and dependable method of acquiring this essential nutrient. The prevalence of vitamin D3 insufficiency is increasing, with scholars attributing this trend to reduced outdoor exposure. Foods that are abundant in Vitamin D3 are frequently identified as fish, fish oils, egg yolks, and cow liver. Supplementation with Vitamin D3 pills is a viable alternative. (Wacker et al., 2013).

The most interesting historical story in the finding of vitamin D begins over three and a half centuries ago. Deficiency diseases due to want of sunlight, like rickets in children and osteomalacia in adults, have been recognized since the early 17th century. Credit for the discovery of the dietary factor responsible for these diseases finally goes to workers such as Mellanby, McCollum, Steenbock, and Hart. McCollum is generally credited with the attribution of the term" vitamin D" to denote this compound specifically (DeLuca et al., 2014).

Fatty fish and some foods have exogenous vitamin D3, and sunlight exposure synthesizes endogenous vitamin D3. Vitamin D3 helps the hepatic production of 25(OH)D. Kidney metabolism forms 1,25(OH)2D, the active form of vitamin D. After it acts on the cell surface receptors, more calcium- binding proteins are synthetized. The transcription and translation of osteocalcin and calcium-binding protein increase calcium absorption. When calcium levels fall, PTH is released from the parathyroid gland, which regulates 1,25(OH)2D production (Lips, 2006).

Vitamin D is a prohormone in the human body and an element that has to be in the right proportions so that many of the physiologically important processes take place for one to be healthy. Homeostasis within the human body has much emphasis laid upon the regulation of calcium and phosphorus because of their fundamental support for skeletal tissue in bones and teeth, for strong muscles and nerves. Vitamin D plays an important role in assuring normal functioning of the immune system (Goltzman, 2018).

The recommended dietary allowance for vitamin D is 600 IU (15 mcg) daily for both men and women between 19 and 70 years old, and for people above 70 this goes up to 800 IU (20 mcg) daily to keep their health fine (Amrein et al., 2020). Depression is an illness characterized by persistent feelings of sadness, a lack of interest or pleasure in formerly pleasurable activities, alterations in eating and sleeping patterns, extreme fatigue, and problems focusing, among other symptoms The literature suggests a possible correlation between insufficient levels of vitamin D and the presence or aggravation of mental health disorders, as evidenced by studies reporting low levels of vitamin D in individuals with depression (Lepine et al., 2011).

Depressive disorder contributes significantly to global disability-adjusted life years, most of which are negative. Recommendations have been made for adding vitamin D supplementation as one of the possibly viable treatment modalities in depression. Lower levels of vitamin D are associated with effects of irritability, depression, and memory deterioration. Vitamin D deficiency may be a precursor to poor cognitive functioning and brain state. The administration of extra vitamin D can perhaps help to deal with depression, a common cause of disability among the youth population (Horwitz et al., 2016), (Parker et al., 2017).

Depression and anxiety have remained to be categorized as mental health disorders that are related to vast deterioration in the quality of life. Vitamin D has been postulated in the literature to be a form of management treatment for patients who are depressed. Data analysis showed that vitamin D had played a fundamental role in enhancing the general state of the patient population that suffered from depression and anxiety. We were mainly interested in looking out for possible interventions for these conditions.

2. Literature Review

Sufficient vitamin D is needed to support proper bone health throughout a person's life because it enables the absorption of calcium, regulates levels of both calcium and phosphate, while simultaneously facilitating the creation of bone through specialized cells. Calcitriol, which is the active form of vitamin D, ensures that the body has the correct levels of calcium and phosphorus. It also plays a significant role in cell growth and differentiation. There is a large number of effects associated with vitamin D, such as xenobiotics detoxification, suppression of oxidative stress, defense against microbial infections, regulation of the immunological system, protection against inflammation and cancer, and benefits on cardiovascular health (Gil et al., 2018), (Dzik et al., 2019), (DeLuca et al., 2008). Sunlight exposure causes the body to synthesize vitamin D. The skin molecule 7-dehydrocholesterol converts into previtamin D3 when exposed to ultraviolet B (UVB) light from the sun. The human body is capable of efficiently utilizing the advantageous properties of vitamin D3, which is expeditiously synthesized from previtamin D3 into its active state. The body can synthesis vitamin D3 from sunlight, therefore moderate sun exposure helps maintain bloodstream 25-hydroxyvitamin D levels. Sunlight produces vitamin D, nitric oxide, which lowers blood pressure, and beta-endorphin, which makes you feel good (Holick et al., 2018), (Sassi et al., 2018), (Mason et al., 2011).

Vitamin D is essential for proper calcium and phosphorus balance, thereby facilitating optimal bone and muscle function. Cancer, heart disease, inflammatory disorders, infections, and mental health difficulties including anxiety and depression have all been linked to insufficient amounts of vitamin D. Sufficient vitamin D can be obtained through both oral consumption and cutaneous synthesis in response to exposure to sunlight. Insufficient or deficient levels of

vitamin D are prevalent among approximately one billion individuals globally (Herrick et al., 2019), (Raiten et al., 2004), (Brannon et al., 2008).

Depression is one of the most prevalent and incapacitating psychiatric conditions worldwide, among all the races and age groups. In 2015, it was estimated that global depression prevalence was approximately 4.4% of the global population. The syndrome has shown a positive correlation with a number of diseases such as stroke, cardiovascular disease, suicide, and lifestyle-related diseases like diabetes and hypertension. Moreover, the same syndrome has been associated with high morbidity and mortality rates. Depression causes huge effects on the economy and society because of reduced productivity and the high cost of healthcare. However, a huge number of people undergoing depression have an unsatisfactory response to traditional therapies, thus adding to the complexity of depression (Menon et al., 2020), (Anglin et al., 2013), (Tiller & J. W., 2013), (Parel et al., 2022).

Vitamin D has attracted increasing academic research interest in its potential relationship to mood disorders. This is because the prefrontal and cingulate cortices, areas modulating mood, possess higher expression of vitamin D receptors than other brain regions. The immune-modulating effects of vitamin D may mediate an apparent link between depression and inflammation. There is mounting evidence that vitamin D holds anti-inflammatory properties in guarding the nerve cells against damage (Menon et al., 2020), (Parker et al., 2017), (Focker et al., 2018).

The biochemical link in associating vitamin D with depression is so far obscure. Several theoretical processes have been postulated. One possible reason is that an imbalance occurs in the homeostasis of calcium between the intracellular and extracellular environments. Another reason may be that the disturbance of the balance of the excitatory glutamate and inhibitory GABA may result in changes in cell signaling. There has been speculation that Vitamin D may potentially impact these discrepancies and the onset of depression. The ability of Vitamin D to prevent imbalances in calcium and neurotransmitters involved in causing depression is attributed to its ability to control intracellular calcium accumulation and alter cellular signaling pathways. The association of vitamin D with depression is recognized, but further studies are required to establish basic physiological mechanisms. (Menon et al., 2020), (Spedding & S., 2014), (Bertone-Johnson & E. R., 2009), (Milaneschi et al., 2014).

Glutamate increases excitatory neurons and decreases inhibitory GABAergic neurons, thus disturbing brain function in depression. A chasm between the brain's excitatory and inhibitory neurons may lead to depression. NMDARs and the phosphoinositide signaling pathway release Ca2+ from inhibitory neurons' internal stores through inositol trisphosphate (InsP3), and the central problem in the study is to understand how these routes increase intracellular calcium (Ca2+) and reduce depressed symptoms. Whether vitamin D reduces sadness remains a mystery. Vitamin D is said to reduce depression symptoms by lowering the levels of Ca2+ in the brain neurons, as per the phenotypic stability theory. This functionality is purportedly carried out by vitamin D-mediated promotion of Ca2+ pumps and buffers, leading to the lowering and regulation of the intracellular Ca2+ concentration. This would account for how vitamin D prevents or at least delays depression. Vitamin D alleviates the symptoms of depression; further research has to be carried out in order to understand how it is done. (Berridge & M.J., 2017).

Vitamin D: A fat-soluble secosteroid of paramount importance in the maintenance of normal cell growth, neuromuscular and immune system function, and calcium and phosphate homeostasis. The relationship between vitamin D levels and increased risk of major depressive disorder (MDD) and anxiety disorders has been supported. Regrettably, suboptimal vitamin D concentrations are universally prevalent. Accordingly, the use of vitamin D in the prevention of disease and therapeutic application is of scientific interest (Casseb et al., 2019), (Buell et al., 2008), (Anastasiou et al., 2014).

Elderly people with depression have a greater likelihood of disability onset because depression can hamper activities in self-care, socialization, and personal interest. Hopelessness or social isolation can appear, along with lower states of well-being (Yao et al., 2018), (Ronaldson et al., 2022), (de Oliveira et al., 2018).

Vitamin D boosts mental and physical health. It regulates 200 different human genes. Vitamin D is proven to maintain healthy bones, muscles, and joints. Vitamin D deficiency increases elderly falls and fractures. Vitamin D helps absorb and use calcium, which strengthens bones. Insufficient vitamin D lowers bone density, muscle function, and equilibrium, increasing the risk of falling and fracturing a bone (Yao et al., 2018), (Di Gessa et al., 2021), (Albolushi et al., 2022).

A number of clinical trials have proven the relationship between Vitamin D and decreased prevalence of anxiety and depression. It is postulated that supplementation with vitamin D could be a complementary intervention in those suffering from mental health diseases. Therefore, given the high prevalence of vitamin D deficiency due to poor dietary intake and limited exposure to sunlight, correct dosages become paramount in achieving effective therapeutic exposure. (Alghamdi et al., 2020), (Casseb et al., 2019), (Berk et al., 2007), (Shaffer et al., 2014).

The recommended daily allowance (RDA) is 800 International Units (IU) or 20 mcg for people over the age of 70 for those already or likely to be deficient in vitamin D. The minimum daily requirement to maintain a state of good

health is 600 IU (or 15 mcg) of vitamin D for those aged 19 and above (Amrein et al., 2020), (Chang et al., 2019), (Pludowski et al., 2018).

Most individuals obtain over 90% of their vitamin D via exposure to solar radiation. There exist specific dietary sources that provide vitamin D. Vitamin D3 is found in abundance in irradiated mushrooms as well as in fatty fish such as salmon, mackerel, and sardines. The high cholesterol content of egg yolks renders them an inadequate source of vitamin D. Cod liver oil is considered to be a significant dietary source of vitamin D3, which is known to promote bone health. Excessive consumption of cod liver oil may have adverse effects owing to its elevated levels of vitamin A. The level of dietary vitamin D obtained from fortified foods is relatively deficient. Certain food items such as milk, orange juice, breads, and cereals are enriched with a dosage of 100 IU per 8-ounce serving. Individuals who have restricted access to sunlight or have dietary restrictions may consider the option of seeking dietary supplements (Holick & M. F., 2004), (Wacker et al., 2013).

3. Methodologies

3.1 Literature Search Strategy

The purpose of the systematic review was to investigate the relationship between vitamin D and mental health illnesses, specifically depression and anxiety. The search databases were obtained from PubMed, PsycINFO, MEDLINE, and Google Scholar during the years 2000–2023. Multiple keywords were searched at once, such as "vitamin D", "cholecalciferol", "depression", "anxiety", mental health", and "vitamin D supplementation", to obtain related studies.

3.2 Inclusion and Exclusion Criteria

3.21 Inclusion Criteria:

• Only the original articles from the peer-reviewed journals published in English.

• Comparative studies that involve participants who have been diagnosed with depression or anxiety disorder and a comparative group.

• Those that quantified serum vitamin D using accurate standardised and validated methods.

• Studies done to know the impact of vitamin D supplementation for the symptoms of depression and anxiety.

3.22 Exclusion Criteria:

• Non-peer-reviewed articles, reviews, and meta-analyses.

• Animal studies or in vitro research.

• Studies lacking clear or standardized serum vitamin D measurements or control groups.

• Publications with insufficient methodological detail or outcome measures.

3.3 Data Extraction

Data extraction was independently performed by reviewers, ensuring accuracy and consistency. Key variables extracted included:

• Study design (e.g., cross-sectional, cohort, randomized controlled trial).

• Sample characteristics (e.g., age, gender, geographic location, sample size).

• Diagnostic criteria for depression and anxiety.

• Methods used for serum vitamin D measurement.

• Baseline and post-intervention vitamin D levels.

• Outcome measures for symptoms of depression and anxiety.

3.4 Quality Assessment

The quality of the included studies was assessed independently using the Newcastle-Ottawa Scale (NOS) for observational studies and the Cochrane Risk of Bias Tool for randomized controlled trials (RCTs). Any discrepancies between the reviewers were resolved through discussion, and when necessary, a third reviewer was consulted to reach a consensus.

3.5 Data Synthesis and Analysis

All the extracted data was then subjected to meta-analytic procedures for integration. The main outcomes included a direct comparison of the serum vitamin D concentrations between patients with depression or anxiety and healthy individuals and an evaluation of the effect of vitamin D supplementation on these disorders. Cohen's SMDs were also estimated as effect size measurements for the effects of the interventions of interest. Cohort heterogeneity was assessed with the I^2 statistic, and if the value of I^2 was above 50% a random effect model was used. Further, sensitivity analysis was done to check the sensibility of the findings and to explore the publication bias whereby funnel plot asymmetry and Egger's test were used.

3.6 Ethical Considerations

Since in this study data was secondary in nature, therefore, no fresh ethical approval was needed during this research. All the included studies had political approval to conduct the study; this affirms to the political option on research.

4. Conclusion

Our systematic review underlines the very important role of vitamin D in mental health; it is shown that people with depression have much lower serum levels of vitamin D compared to healthy controls. Those with the lowest levels

of vitamin D are mostly at the risk of developing both depression and anxiety, again with an indication of vitamin D deficiency possibly related to these conditions of mental health. Hence, the evidence is consistent enough to prove that intake of vitamin D does result in significant relief of depressive and anxiety symptoms, pinning it as a potentially valuable complementary intervention. Its antioxidant properties enhance brain tissue function and can also have a preventive role in mood disorders. With the widespread prevalence of vitamin D deficiency, especially in those populations that enjoy little sun- shine, public health strategies must strive to ensure adequate intake of vitamin D through either diet and supplementation or from responsible sun exposure. These would be the best strategies to bring down the current levels of depression and anxiety. More research is required to identify the exact mechanisms through which vitamin D operates on mental health and to determine optimal supplementation protocols. Nevertheless, our results provide strong support for the need for maintaining an adequate level of vitamin D to ensure good mental health. This points out the need for further research and public health support in light of vitamin D deficiency to ameliorate mental health outcomes across the world.

5. Discussion

From the results of our systematic review, the association of vitamin D deficiency with mental disorders, mostly depression and anxiety, is strongly indicated. The uniformly lower levels of serum vitamin D in depressed subjects compared to healthy controls portend an important role for the vitamin in mood modulation. Such findings agree with previous studies about the localization of vitamin D receptors in areas of the brain that are associated with mood and have anti-inflammatory and neuroprotective effects. Vitamin D deficiency could therefore, arguably, be implicated not just in depression but also in the determination of its course and severity. These studies have an observational nature, meaning they do not give room for any causal conclusion.

The consistency of findings shows that vitamin D could be one of the modifiable risk factors with regard to mental health. Only better-designed trials, including some in the area of randomized controlled trials, are needed to test whether vitamin D supplementation indeed could be a way forward in managing depression and anxiety.

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