

Vitamin D Deficiency and Depression: A Short Review Article

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Context: Depression is a common illness worldwide and results from a complex interaction between social, psychological, and biological factors. Although there are studies reporting a correlation between vitamin D deficiency and mood disorders, a consensus on a concrete link between vitamin D levels and depression has yet to be reached.

Evidence Acquisition: In this short review, we discuss the relationship between vitamin D deficiency and depression. Our literature review yielded 42 articles published since 2006 in the electronic databases of MEDLINE, EMBASE, CINAHL, AMED, and PsycINFO.

Results: This study was conducted on the assumption that low levels of vitamin D are associated with depression. However, for all the evidence indicative of an association between low levels of vitamin D and depression, there is still a great deal of controversy over such correlation due to the current conflicting results. Further research is needed to fully elucidate the issue.

Conclusions: The initial assumption of a relationship between vitamin D and high prevalence of seasonal affective disorder in winter was based on the high prevalence of depression on high latitudes. Although some studies have shown an association between depression and vitamin D deficiency, it still cannot be indisputably concluded that augmenting the levels of vitamin D alone alleviate depression.

Keywords: Vitamin D Deficiency; Major Depressive Disorder; Affective Disorders

1. Context

Major depressive disorder (MDD), also known as unipolar depression, is a serious emotional disease that negatively influences thoughts, feelings, behavior, mood, and physical health and is characterized by the presence of one or more depressive episodes during the patient's lifetime (1). MDD is the third leading cause of disability and recognized as a major determinant of disability, mortality, and health care costs (2). This disorder is a common illness worldwide and results from a complex interaction between social, psychological, and biological factors (3). About 4.4% of the total global disability-adjusted life year (DALY) in 2002 was attributed to this disease. Moreover, it is anticipated that MDD will be the second major cause of disease burden by 2020 (4) and 2030 (5). Sadeghirad et al. showed that the prevalence of MDD in Iran in the year 2010 was 4.1; when compared to the reported rates in other countries, this figure can be interpreted as average level (6).

Depression exerts a significant negative impact on lives and is deemed the fourth leading cause of high DALY rates across the globe. MDD also is bracketed together with significant disability, mortality, and health care costs in high-income countries (7, 8). Patients affected by MDD are liable to derive less pleasure from their activities, experience weight fluctuation, suffer from sleep disorders, feel weary, experience lapses of concentration, and

even feel worthless or guilty. The exact cause of MDD is unknown, and it is probable that several mechanisms are involved (1, 9). However, many researchers believe that MDD is linked to chemical changes in the brain, genetic disorders, or a combination of both. MDD tends to run in families, but sporadic cases have also been reported (1, 2).

There are established types of treatment for MDD: 1) medication; 2) psychotherapy such as cognitive behavioral therapy and interpersonal therapy; 3) combination of medication and psychotherapy; 4) electroconvulsive therapy; and 5) transcranial magnetic stimulation. Additionally, aerobic workout and complementary and alternative medicine are among the other types of treatment. Such methods can be used alone or alongside the traditional methods of healing (10-12).

Vitamin D deficiency is a common health problem, with clinical implications such as cancer, cardiovascular disease, multiple sclerosis, psoriasis, diabetes, and other diseases like schizophrenia and depression (13-15). Heshmat et al. (2008) found that vitamin D deficiency was a common disease in Iran, especially in Tehran, and recommended that this be seriously considered by experts (16).

Vitamin D can be obtained through food consumption or synthesized in the body via sun exposure. A large number of factors such as sunlight exposure, dietary intake, and air pollution have contributed to the high prevalence

of vitamin D deficiency throughout the world, and epidemiological evidence shows that vitamin D deficiency is associated with an 8% -14% increase in depression (17, 18).

When serum 25-hydroxyvitamin D reaches a level < 20 ng per mL (50 nmol per L) in adults, it is said that the person is affected by vitamin D deficiency. Furthermore, a serum 25-hydroxyvitamin D level of about 20 to 30 ng per mL (50 to 75 nmol per L) is defined as vitamin D insufficiency (18). Two types of vitamin D have been identified: ergocalciferol and cholecalciferol. According to the previous findings, nutritional sources alone cannot provide the sufficient amount of vitamin D. As a result, 90% of vitamin D required for the human body is typically provided by sunlight (19, 20). The national academy of sciences, institute of medicine, and food and nutrition board (2004) recommend the following dietary intake of vitamin D: people aged between 1 and 50 years should take 200 international units (IU) of vitamin D; people between 51 and 71 years of age need 400 IU; and people over 71 years old should take 600 IU of vitamin D (21). Many experts believe that these values are too low to support maximal nutritional health and are low in comparison to the amount of vitamin D made endogenously through sun exposure (10,000 to 20,000 IU vitamin D within 24 h of exposure) (Hollick, 2007) (22). Two studies by Heshmat (2008) and Moussavi (2005) showed that Iran is a country with a high prevalence of moderate to severe vitamin D deficiency (16, 22, 23). Elsewhere, Hoogendijk (2008) and Armstrong (2007) showed that vitamin D is mainly used to maintain the concentration of calcium and phosphorus in the blood and that it helps and enhances the cellular, neuromuscular, and ossification performance. In addition, the authors concluded that vitamin D is required for optimal health and may have an important role in the mental health; nevertheless, its relation to depressive symptoms and other psychiatric disorders is unclear and needs further investigation (24, 25). Given the high cost of depression and the controversial relationship between vitamin D and depression, further research into this relationship seems necessary.

2. Evidence Acquisition

In this short review, we probed into the relationship between vitamin D and depression. The literature covers a variety of topics such as the definition for vitamin D deficiency, the criteria for MDD, and the relationship between vitamin D deficiency and depression. We performed the present study on the assumption that a low level of vitamin D is associated with depression. Our literature review in the electronic databases of MEDLINE, EMBASE, CINAHL, AMED, and PsycINFO yielded 42 articles since 2006.

3. Results

Vitamin D deficiency is very common around the world and negatively impacts overall health, especially in the

domain of mental health. Vitamin D is a risk factor for depression. A decrease in the level of vitamin D in the body is allied to several problems such as hypertension, neurodegenerative disease, cardiovascular disease, metabolic syndrome, and diabetes. The initial proposal on the relationship between vitamin D and high prevalence of seasonal affective disorder in winter was based on the high prevalence of depression on high latitudes. With regard to depression, several questions are raised: How does vitamin D deficiency act as a determinant for depression? Is depression caused by vitamin D deficiency? Are the signs of depression alleviated by providing vitamin D for the patients? And, what is the causal relationship between vitamin D level and depression? (26-29). Recent scientific research has scrutinized the connection between insufficient vitamin D and mood disorders and shown a relationship between low levels of vitamin D and the presence of depression. Several investigations have focused on the efficacy of vitamin D supplements in the recovery from depression and indicated a causative relation. Nonetheless, the findings of these trials are inconsistent and the question, therefore, remains as to whether vitamin D deficiency causes depression or whether supplementation relieves depression symptoms or indeed whether lower levels of vitamin D are a cause or consequence of depression (27-29).

Sotodeh Asl et al. (2014), Berk et al. (2007), Hogberg (2012), Mozaffari et al. (2013), Eskandari et al. (2007) and Jorde et al. (2008) demonstrated a correlation between low vitamin D levels and MMD and mood disorders (30-35). low levels of vitamin D are associated with seasonal affective disorder, depression, and schizophrenia in adults, there is conflicting evidence about the relationship between vitamin D deficiency and psychological disorders (30). It has been previously suggested that more attention be paid to vitamin D deficiency in psychiatric disorders. Mozaffari and coworkers in a meta-analysis (2013) demonstrated that the efficacy of vitamin D supplements in depression is controversial and needs further studies. Their results showed that when vitamin D supplements were used, a statistically significant improvement occurred in depression (33). Nevertheless, the results of some other studies were largely questionable; they showed that depression was worsened by vitamin D supplements. Some studies have demonstrated that a change in vitamin levels (vitamin D supplementation \geq 800 IU daily) is somewhat useful in the management of depression and that its impact is comparable to that of anti-depressant medication (33).

Jorde et al. (2008) in a cross-sectional study investigated the effect of serum 25-hydroxyvitamin D on depression among overweight and obese individuals. The authors recruited a group who received vitamin D supplements and one group who received a placebo. At 1-year follow-up, there was a significant improvement in the Beck depression inventory (BDI) scores. Jorde et al. concluded that the depressive symptoms were more significant in

the patients with serum 25-hydroxyvitamin D 25 (OH) D levels of $< 40 \text{ nmol L}^{-1}$ than those with 25(OH)D levels $\geq 40 \text{ nmol L}^{-1}$ (35).

Maddock et al. (2013) in a cross-sectional prospective study concluded that low 25-hydroxyvitamin D concentrations are allied to current and subsequent risk of depression in mid-adulthood. The investigators showed a non-linear ($P = 0.01$) relationship between 25-hydroxyvitamin D and subsequent (50 years) risk of depression. Moreover, their results demonstrated that the patients with 25-hydroxyvitamin D levels between 50 and 85 nmol/L were less at risk than those who had lower or higher concentrations (36). Two studies by Chan (2011) and Pan (2009) showed no relationship between vitamin D and depression (37, 38).

Finally, for all the studies demonstrating an association between low levels of vitamin D and depression, a consensus on a definite link between vitamin D levels and depression has yet to be reached. Further studies are required to shed sufficient light on this issue.

4. Conclusions

The present review is consistent with the hypothesis that low levels of vitamin D are associated with depression. Our literature review showed that a large body of research supports the efficacy of vitamin D supplementation in alleviating depression and indicates that vitamin D may play an important role in mental health and in depression by impacting on the areas of the brain linked to depression. Nonetheless, the mechanism whereby vitamin D works in the brain has yet to be fully illuminated (29-34). Some studies have reported a weak association between vitamin D deficiency and depression, but these studies failed to show a precise causal association between low vitamin D levels and depression. Consequently, it still is not clear whether depression is caused by other factors; and when depression improves, it is difficult to conclude that vitamin D alone has brought about this positive development (39, 40). The reasons behind these inconsistent findings may lie in the fact that these studies had small patient populations and utilized dissimilar methods for the assessment of depression. There is a dearth of evidence in the existing literature on the relationship between low vitamin D levels and depression, and the current guidelines on the prescription of vitamin D supplementation for MDD are far from being incontrovertible; there is, accordingly, a need for further research into this issue (27, 41-43).

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Authors' Contributions

Nemat Sotodehasl: idea and search for previous related articles. Farhad Malek: idea and preparation of the paper

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