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THE ASSOCIATION BETWEEN VITAMIN D AND MENTAL HEALTH: A NARRATIVE REVIEW

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Abstract:

The present study aimed at providing a narrative description of the studies assessing the association between vitamin D and mental health. A review of the studies published in the period between 2015 and 2022 using different electronic databases (PubMed, CINAHL, Embase) was performed. The results of the studies revealed that vitamin D was associated with different mental health issues, mainly depression, Alzheimer's disease, cognitive disturbances, suicide and autism spectrum disorder (ASD). The findings of the study showed that both vitamin D deficiency and insufficiency were risk factors for the development of these mental health disorders or even in the severity of the symptoms of these disorders. The study concluded that low levels of vitamin D is a significant factor associated with increased risk of mental health disorder. The study recommends conducting further randomized-clinical trials to further assess the association between vitamin D and mental health disorders.

Keywords: *Vitamin D, Mental Health, Narrative Review, Cognitive impairment*

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INTRODUCTION:

The intake of sufficient vitamins helps both physical and mental health. When it comes to health and nutrition, it is impossible to separate our minds from our bodies as when is neglected, the other may suffer (Aggarwal et al., 2022). Taking vitamins that support a healthy body can also support mental health and brain function. When our bodies experience certain vitamin deficiencies, it can cause our organs to grow weak and work less effectively (Wells et al., 2021).
Several important vitamins and minerals support the body's biochemical reactions and promote the healthy function of brain cells and neurotransmitter pathways (Tardy et al., 2020). Vitamin D is a group of fat-soluble secosteroids (responsible for increasing intestinal absorption of calcium, magnesium, and phosphate, and multiple other biological effects) (Silva, 2022). Vitamin D is highly active in regulating cell differentiation, proliferation, and peroxidation in a variety of structures. Vitamin D is crucial not only for bone health but for proper brain development and functioning. Receptors for Vitamin D are present in most cells of the body including the brain (Zmijewski, 2019).

Vitamin D deficiency is most defined by most experts as lower than 20ng/ml. it is associated with an increased risk of depression from 8% to 14% and a 30% increased risk of suicide (Chen & Konkle, 2020). Vitamin D, also known as the sunshine vitamin, is one of the most important nutrients needed by human body. It does not only affect individual's immune system and bones, but it is also important for mental health (Alia & Kerr, 2021).

Lerner et al (2018) reported that there is a significant association between vitamin D deficiency and different mental disorders as reported in literature. However, the study reported that there is no research-based evidence that using vitamin D supplements improves the mental health status or reverse the symptoms of mental health disorders.

In another study by Föcker et al (2017), the researchers conducted a systematic search of PubMed databases and found that all the retrieved studies, either cross-sectional, longitudinal, randomized clinical trials, or systematic reviews revealed that vitamin D plays a significant role in the pathogenesis of mental health disorders among children and adolescents.

Cuomo et al (2019) carried out a study that aimed at investigating the prevalence and predictors of vitamin D deficiency in a sample of 290 hospitalized patients who are mentally ill. The findings of the study showed that vitamin D deficiency is prevalent among about 94% of the enrolled mentally ill patients. In addition, it was found that physical activity and diet were predictors of vitamin D levels. In addition, Tsiglopoulos et al (2021) carried out a systematic review that aimed at providing a research-based evidence about the association between vitamin D and symptom domains in psychotic disorders. The study included 29 articles after the applying the eligibility criteria and quality assessment procedure. The results of the study showed that lower vitamin D serum levels were inversely associated with the severity with symptom domains in people with psychosis.

Despite the intensive research studies exploring the association between vitamin D serum levels and mental health status, still this issue is an argumentative issue due to the variation in the findings and effects of low vitamin D on the severity of the symptoms. Therefore, the present study aimed at providing a narrative review of the studies discussing the effect of vitamin D deficiency on the mental health status through providing different themes based on the type of the mental health disorder.

Vitamin D and Depression

The idea about the link between the deficiency of vitamin D and depression comes from studies dealing with seasonal affective disorder. Low serotonin levels in the brain have been linked to the symptoms of seasonal affective disorder. Vitamin D treatment was associated with improved depression symptoms measured by the Hamilton Depression Scale.

Ceolin et al (2021) conducted a study that aimed examining whether vitamin D deficiency or insufficiency is associated with depression whether vitamin D supplementation is an effective treatment for depression. A systematic literature review study was performed through using different databases and specific keywords. The results of the study showed that there is a strong evidence about the association between vitamin D insufficiency and depression.

In some cases, depression can be a symptom of a psychological vitamin D deficiency. The British Journal of Psychiatry confirmed a link between low levels of vitamin D in the body and an increased chance of depression (Ronaldson et al., 2020).

The Journal of Chemical Neuroanatomy also published that vitamin D has an effect similar to the effect of neurosteroids in the brain, in addition to the proliferation of vitamin D receptors in brain tissue, and its ability to secrete hormones and chemical

compounds responsible for transmitting signals among the cells (Autocrine), and therefore its deficiency from the required level may lead to the emergence of psychological symptoms (Anjum et al., 2018). Psychological symptoms associated with depression include: mood changes accompanied by feelings of hopelessness and sadness, general tiredness and exhaustion, excessive forgetfulness, loss of interest in activities that the person usually wants to do, suicidal ideation, loss of appetite, excessive weight loss or gain, insomnia (Anjum et al., 2018).

Schaad et al (2019) carried out a retrospective review of records study that aimed at investigating the association between vitamin D serum levels and depression among athletes. The findings of the study showed that depression was more prevalent among athletes who had vitamin D deficiency (about 20% of the study sample were diagnosed with depression based on the diagnostic codes used in this study).

Moreover, Jahrami et al (2020) performed a case-control study that aimed at estimating the cumulative doses of vitamin D from solar or diet resources among patients diagnosed with depression compared to normal individuals. It was found that patients who were diagnosed with depression received lower vitamin D doses from solar or diet resources and these doses were lower than normal recommended doses.
In Wong et al (2018) study aimed at reviewing the research-based evidences about the association between vitamin D deficiency and depression. The systematic search process included the adoption of a search protocol of different databases. The findings of the study showed that there is an increasing evidence that vitamin D deficiency is significantly associated with increased severity of depression.

In addition, Menon et al (2020) carried out a study that aimed at evaluating the available evidences about the association between vitamin D and depression. A systematic review was conducted through searching the databases for evidences published in the period until 2019. The results off the study revealed that there is an inverse association between vitamin D serum levels and clinical depression. However, there is no sufficient evidence about the effect of vitamin D supplements in reducing depressive symptoms or depression.

Vitamin D and Suicide

It has been known that suicide is a global health concern and takes about 1 million lives every year worldwide (Yagci & Avci, 2021). Some psychiatric researchers reported an asymmetry in the seasonal distribution of suicide, with a peak in the late spring months for both sex. Increased risk of suicide in areas with less sun exposure, and in the spring with low vitamin D serum levels. In addition, it was found that highest risk of suicide was among people having vitamin D serum levels that is less than 15.5ng/ml (Gokalp, 2020).
Two studies addressed this issue, the first one dealt with suicide cases (n=495) to be matched with control subjects (n=495). It was found that more than 30% of all subjects had vitamin D values below 20 ng/ml. the study concluded that lowest vitamin D serum levels are associated with an increased risk of suicide (Umhau et al., 2013).

Another study used a sample of 59 suicide attempters and a sample of 17 Non-suicidal depressed patients and 14 healthy controls. This study came up with a conclusion that suicide attempters had significantly lower mean levels of Vitamin D (O'Connor, 2021). In a study conducted by Goklap (2020), the purpose was to examine the association between low vitamin D levels and suicidal attempts. The sample of the study consisted of 215 patients attending the pediatric emergency department. The findings of the study revealed that vitamin D deficiency is significantly associated with suicidal behaviors among adolescents and could be one of the causes and risk factors.

Kim et al (2020) performed a cross-sectional study that aimed at identifying the association between vitamin D deficiency and suicidal ideation. A sample of 157.211 blood samples from Korean adults were tested. The results of the study showed that deficient vitamin D levels were significantly associated with increased risk of suicidal ideation. However, the study found no significant statistical differences between both vitamin D insufficient and sufficient groups.

Vitamin D and Schizophrenia

Schizophrenia is a chronic and severe mental disorder or brain disorder characterized by abnormal social behavior and affects the person's thinking and feelings (Binder, 2021). In addition to conventional schizophrenia theories, there is a hypothesis concerning vitamin D as a component of its pathogenesis. In order to prove this theory, animal models were developed and it was proved that vitamin D receptors are directly involved in the regulation of dopaminergic-associated genes expression (affect dopamine production) (Shayganfard, 2021). Moreover, it was found that vitamin D deficiency during embryonic development is a risk factor for schizophrenia. This is because an epidemiological link has been observed between disease after birth, latitude,

and occurrence of this mental disorder. It is believed that this distribution of vitamin D receptors in certain brain regions suggested that vitamin D is associated with particular neurotransmitters and cortical function (Freedman et al., 2021).

Studies have shown that the lack of vitamin D can affect individual's brain in many ways. Even among relatively healthy people, vitamin D deficiency has been linked to reduce memory and function (Anjum et al., 2018). One recent study showed why vitamin D is vital for brain health and how its deficiency can lead to disorders including depression and Schizophrenia (Okasha et al., 2020). In the study, researchers were moved to find it indeed from the diet of a healthy group of adult mice and after 20 weeks found a significant decline in their ability to remember and learn compared to a control group. Researchers found that the vitamin D deficient group had reduced peri-neuronal networks in the hippocampus, which is the brain region crucial to memory formation (Mayne & Burne, 2019). These networks act as a scaffolding for the brain. They stabilize important neurons and the connections between them. Researchers proposed that Vitamin D plays an important role in keeping these nets stable, and that when vitamin D levels drop, this scaffolding is more easily degraded by enzymes. Loss of function in this area could be an important contributor to the hallmarks of Schizophrenia including severe memory deficits and distorted perception of reality (Trifonova et al., 2019).

Zhu et al (2020) carried out a systematic review study that sought to provide a research-based evidence about the association between Schizophrenia and vitamin D serum levels. This review included a total of 36 articles retrieved from different databases through a systematic search of the electronic databases. The results of the study showed that Schizophrenic patients were more likely to have vitamin D deficiency or insufficiency compared to normal individuals.

Eyles et al (2018) carried out a case-control study that aimed at testing the hypothesis stating that "prenatal vitamin D deficiency could increase risk of schizophrenia". The sample of the study included a sample of 2602 participants. Serum vitamin D levels were assessed in neonatal dried blood sample. The results of the study showed that there is a significant association between vitamin D serum levels and increased risk of schizophrenia.

Lally & Gaughran (2019) conducted a clinical review of the evidences available about the association between vitamin D deficiency and both depression and schizophrenia severity. The findings of the study showed that despite that there are a number of observational studies ensuring the association between vitamin D levels and schizophrenia and depression, still there is an urgent need for more randomized clinical trials investigating the nature and the strength of this association.

Siddiqui et al (2018) conducted a narrative review study that aimed at assessing the previous findings related to the association between vitamin D deficiency and schizophrenia among elderly patients. The study primary outcome revealed that neonatal vitamin D deficiency is significantly associated with development of schizophrenia at later life. In addition, it was found that vitamin D deficiency increases the severity of the symptoms of schizophrenia among elderly patients.

Vitamin D and Cognitive Disturbances

Some of the cognitive disorders that have been found to be in association with vitamin D are Dementia and Alzheimer's disease. More than ten percent of people over 65 years old and 50% of people over 85 years old develop dementia (Bivona et al., 2021). In addition, Alzheimer's disease is a chronic neurodegenerative disease and represent 60 to 70% of these cases. The experimental studies revealed abnormal morphology in low vitamin D, have longer cortex, increased brain size, reduced expression of nerve growth, increased cellular proliferation. In another study, subjects with vitamin D serum levels less than 50nmol/L will more be twice to have all-cause dementia or Alzheimer's disease (Agnihotri & Aruoma, 2020).

Miller et al (2015) looked at vitamin D and cognitive function in an elderly cohort and this cohort was at the University of California – Davis Alzheimer's disease center. The study was begun in 2002 and ended in 2010, there were 382 participants at the beginning of the study and consisted of 60% African American or Hispanic and 40% were white and there were few other races and ethnicities involved. The people were about 75 years of age at the beginning of the study and they were either cognitively intact or they had mild cognitive impairment or some had outright dementia. The researchers looked at vitamin D status at the beginning of the study at baseline and then the researchers followed their cognitive function over time for an average of five years for the group. None of the subjects were on vitamin D supplements, researchers were looking at their vitamin D status as it came from diet and from sunlight exposure. It was found that about 60% or more of the participants were low in vitamin D, either insufficient or outright deficient. Deficiency is defined as less than 12ng/ml

and insufficiency is between 12 and 20ng/ml in the blood. African-Americans and Hispanics on average had lower vitamin D status than the white subjects in the study.

Toffanello et al (2014) conducted a study that discussed vitamin D deficiency and whether it can be used as a measurement of how people are doing cognitively and a possible early dementia signs. The study took over 1900 elderly subjects and they measured their 25-hydroxy vitamin D levels. The participants were given a mental state examination, which is a standardized examination given for a cognitive function. Interesting findings were that subjects with a vitamin D level less than 50nmol/L (deficiency) or less than 75nmol/L were more likely to have declining cognitive function scores, which means that they were more likely already showing early signs of dementia.

According to a study published in the Journal of gerontology, researchers at Duke in U.S medical school and Duke University have associated low vitamin D levels with an increased risk of cognitive decline in the elderly. The results reinforced the importance of identifying vitamin D insufficiency among the elderly. Low vitamin D levels were associated with significantly faster rates of decline in memory and executive function performance (Matchar et al., 2016). In addition, a study published in JAMA neurology demonstrated a significant association between vitamin D insufficiency and cognitive decline specifically seen with Alzheimer's disease and dementia. Research continues to show the significant role of vitamin D plays in our overall health. However, the current research also demonstrates its significant role in maintaining healthy brain function. The study, which included twelve hundred and two participants who were 60 years or older is the first large-scale study in Asia to examine the association between vitamin D status and risk of cognitive decline and impairment in the elderly. Their baseline vitamin D levels were measured at the start of the study and their cognitive abilities were assessed over a two-year period. As a result, individuals with lower vitamin D levels at the beginning of the study were about twice as likely to display significant cognitive decline over time. In addition, low vitamin D levels at baseline also increased the risk of future cognitive impairment. This research reinforces that vitamin D protects against neuron damage and its effects on cognitive decline (Kahwati et al., 2021).

Vitamin D deficiency is a common problem that has many health consequences. Yet, it can easily be addressed. Sun exposure is the ideal source of vitamin D, but the reality is most individuals have low vitamin D levels and require supplementation (Remelli et al., 2019). Many people avoid the sun due to the danger of overexposure, so they will cover up potentially exposed skin with either clothing or sunblock. In addition, many of life's obligations require us to spend countless hours inside under fluorescent lights and away from natural light. Also, both latitude and time of year will influence the amount of vitamin D that can be obtained from the sun and in some locations, these limitations may be hindrances throughout most of the year (Aparna et al., 2018).

Vitamin D and Autism Spectrum Disorder (ASD)

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder caused by a complex interaction between genetic and environmental risk factors. ASD is characterized by impaired social interaction and impaired verbal and non-verbal communication (Santos et al., 2022). ASD is accompanied by restricted and repetitive behavior patterns. In Asia, Europe, and North America, ASD prevalence ranges from 6 to 10 per 1000 children. Different studies reported that among ASD children with lower concentrations of vitamin D, there was an increased brain size, altered brain shape, enlarged ventricles (Mazahery et al., 2016). In addition, it was found that maternal vitamin D deficiency is a risk factor for ASD. Various studies reported that vitamin D supplementation decreases the risk of severity of autism and the mechanism of action includes anti-inflammatory activity and autoimmune effects. Using vitamin D supplementation for ASD children was found to improve aberrant behavior, eye contact and attention span outcomes (Feng et al., 2017). Moreover, a study by Siracusano et al (2020) reported that supplementing infants with vitamin D might be safe and more effective for reducing the risks.

In a systematic literature review conducted by Wang et al (2020), the researchers sought to provide a research-based evidence about the association between vitamin D and ASD. A total of 34 research papers were found to be eligible and included in this systematic review data extraction. The results of the study showed that there is a significant association between the level of vitamin D status and risk of ASD. The study recommended designing appropriate interventions to assess vitamin D deficiency among lactating women and their infants at early stage of life. In addition, Kittana et al (2018) found that using vitamin D supplements significantly reduces the risk of ASD but the effectiveness of the supplements was age-dependent as reported in the reviewed studies.

In a case-control study performed by Windham et al (2019), the researchers examined the blood serum vitamin D levels of newborns of the years 200 to 2003. The study included a sample of 563 children who were diagnosed with ASD and 190 children who were diagnosed with intellectual disabilities. The findings of the study showed that there is no significant association between lower levels of vitamin D and increased risk of either ASD or intellectual disabilities. The study recommended conducting further case-control, observational and randomized clinical trials to identify the association between vitamin D deficiency and mental health disorders in general and ASD and intellectual disabilities in particular.

CONCLUSION:

Vitamin D plays an important role in many functions of human body, including regulation of bone density, immune health, cardiovascular health and neuromuscular function. The role of vitamin D in the body is to maintain healthy bones and teeth by helping the individual absorb calcium and phosphorous from food. Inadequate intake of vitamin D has been linked to a myriad of health problems from bone disease to cancer. Vitamin D has an important role in mental health and disease prevention. Vitamin D deficiency also increases the risk of depression, dementia, Alzheimer's disease and other mental and non-mental health disorders. It is also associated with different neurodegenerative diseases like Alzheimer's disease, Parkinson's disease and multiple sclerosis.

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