Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(6), 464-473 | ISSN:2251-6727

Vitamin D Deficiency and Psychotic Features in Mentally Ill Patients: A Systematic Review

Mohammed Ghannam Thallab Alharbi1, Areen Amer A Alenezi2, Razan Atallah Q Alanazi2, Wahaj Amer A Alanazi2, Dhay Ayed A Alruwaili2

1Internal medicine consultant, Prince mohammed Medical city, Riyadh, Saudi Arabia

2Medical intern, Faculty of Medicine, Northern Border University, Arar, Saudi Arabia

(Received: 16 September 2024 Revised: 11 October 2024 Accepted: 04 November 2024)

KEYWORDS

Anxiety; Depression; Young adults; Causes; Risk factors; Management Systematic review.

ABSTRACT:

Objectives: To compile the literature's findings and shed light on how vitamin D deficiency affects psychological traits in individuals with mental illnesses

Methods: A thorough search of pertinent databases was done in order to find studies that satisfied the requirements for inclusion. A thorough search of PubMed, Web of Science, SCOPUS, and Science Direct was conducted to find pertinent literature.

Results: Fifteen studies, including a total of 2196 participants diagnosed with psychiatric illness, and 1115 (50.8%) of them were males, were included in our data. The prevalence of vitamin D deficiency among patients with mental illnesses ranged from 22% in schizophrenia patients to 76% in AD patients. In AD patients, vitamin D may be useful short- and long-term predictors of cognitive deterioration, motoric cognitive risk, and depression. In bipolar patients, a manic episode may be triggered by a decreased vitamin D level and the worsening of depression. Patients with first-episode schizophrenia should have their plasma vitamin D levels tested, particularly if they have a longer duration of untreated psychosis and more pronounced negative and severe depressive symptoms.

Conclusion: Low vitamin D levels are found in neurological and psychiatric patients, but the significance of these findings is not entirely clear because low vitamin D levels are also frequently found in healthy subjects or because several study flaws severely reduce the significance of the findings. Future studies' primary objective would be to map out the variables affecting supplementing efficacy and identify people who benefit from taking vitamin D analogs. This may contribute to the advancement of vitamin D understanding to practical therapeutic needs.

Introduction

One naturally occurring substance that is a member of the steroid hormone class is vitamin D. A tiny quantity of active Vitamin D can also be obtained by diet, although humans synthesize it from a precursor found on the skin. When vitamin D was discovered in a variety of organs, tissues, and cytotypes that both produced and received the hormone, its metabolism was drastically altered. This discovery occurred at the beginning of the 20th century. It originated during the period known as Vitamin D "non-skeletal activities," when a growing body of research revealed the hormone's functions, including the control of immunological response and brain function [1].

The idea behind looking for a possible connection between these disorders and vitamin D was that the hormone could affect and change a number of brain functions, such as the degree to which certain brain circuits related to memory, emotion, and thought processes are connected. It can also control a wide range of immune responses from T helper cells' cytokine generation to the antimicrobial activities of neutrophils and macrophages in both the innate and adaptive arms of immunity. Regular measurements of vitamin D circulating levels in autoimmune disease patients have shown, among other things, a wide range of variations in the frequency and severity of some pathologies, as well

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(6), 464-473 | ISSN:2251-6727

as a high frequency of low vitamin D concentrations in these patients [2].

It is suggested that vitamin D functions as a membrane antioxidant. Additionally, it raises the levels of antioxidant agent gene expression [3]. By inhibiting the activation and expression of nuclear factor kappa B (NF-κB) and other associated genes, vitamin D also reduces the synthesis of cytokines [4]. Based on available data, vitamin D may enhance behavior and mood by influencing the synthesis of neurotrophic factors and neurotransmitters [5].

The purpose of this systematic review was to compile the literature's findings and shed light on how vitamin D deficiency affects psychological traits and mental health measures in individuals with mental illnesses by synthesizing current literature, identifying knowledge gaps, and offering insights for future research and clinical practice

Methods

We followed the recommendations in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [6] for this systematic review. An electronic search was performed on databases like PubMed, Web of Science, SCOPUS, and Science Direct in order to find English-language research. Relevant keywords were included in the search strategy for these situations; “mental disorders,” “Psychiatric disorders,” “Vitamin D levels,” “Hypovitaminosis D,” and “25 (OH) D.” Independently, reviewers went through the search results, chose pertinent papers, collected data, and used the right assessment methods to determine how good the included research was.

Eligibility Criteria:

Inclusion Criteria:

1. Studies published in the English language.
2. Studies reported the association between vitamin D levels and psychiatric disorders’ progression.
3. Studies reported the association between vitamin D levels and psychiatric features.
4. Only adults aged >18 years.
5. Studies involving human participants.
6. Randomized controlled trials, cohort studies, case-control studies, and cross-sectional studies.

Exclusion Criteria:

1. Studies not published in English.
2. Animal studies, in vitro studies, and review articles without original data.
3. Studies with insufficient data or unclear methodology.
4. Case reports and case series with fewer than five participants.
5. Studies with overlapping data or duplicate publications.

Data Extraction

Rayyan (QCRI) was used to validate the search results in order to guarantee accuracy [7]. The inclusion and exclusion criteria were used to determine the relevancy of the titles and abstracts that the search produced. Papers that satisfied the inclusion requirements were carefully examined by the study team. Consensus was used to settle disagreements. Using a predetermined data extraction form, key study data, such as titles, authors, publication year, study location, gender distribution, participant demographics, diagnostic tool of psychiatric features, diagnostic tool of vitamin D level, type of psychiatric disorder, prevalence of vitamin D deficiency, and main outcomes were documented. To evaluate the possibility of bias, an impartial assessment instrument was created.

Data Synthesis Strategy

Summaries of the research findings and elements were created utilizing information taken from pertinent studies in order to offer a qualitative assessment. The best method for making use of the data from the studies that were included was decided upon after the data collection for the systematic review was finished.

Risk of Bias Assessment

The Joanna Briggs Institute (JBI) [8] critical assessment criteria for studies reporting prevalence data were utilized to assess the study's quality. This tool had nine questions. A score of one was given for a positive

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(6), 464-473 | ISSN:2251-6727

response, while a score of zero was given for a negative, ambiguous, or irrelevant response. The following scores will be categorized as low, moderate, and high quality, respectively: below 4, between 5 and 7, and above 8. The quality of the studies was evaluated by researchers independently, and differences were settled through discussion.

Results

Systematic search outcomes

After 798 duplicates were removed, a total of 1314 study papers were found through a systematic search. After 516 studies had their titles and abstracts evaluated, 456 papers were discarded. Merely 2 articles were not located out of the 60 reports that were required to be retrieved. 58 articles passed the screening process for full-text evaluation; 10 were rejected due to incorrect study results, 31 due to incorrect population type, and 2 articles were editor's letters. Fifteen research publications in this systematic review satisfied the requirements for eligibility. An overview of the procedure used to choose the research is illustrated in **Figure 1.**

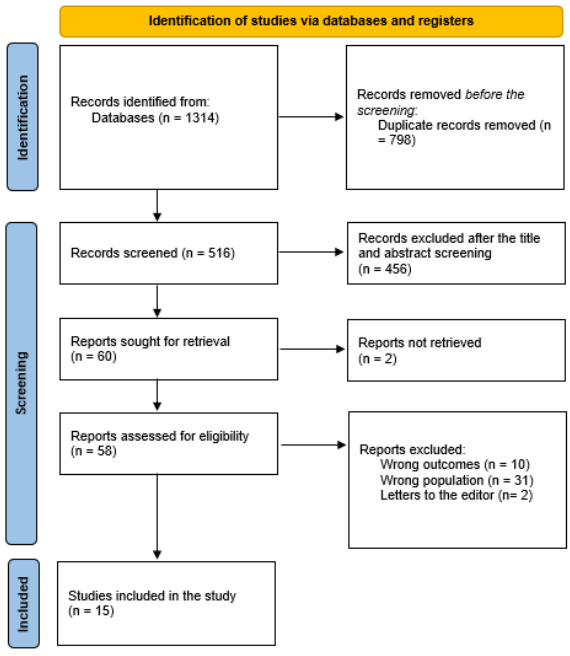

Figure (1): Study decision is summed up in a PRISMA diagram.

Sociodemographic features of the comprised studies

The research publications' sociodemographic information is displayed in **Table 1.** Fifteen studies, including a total of 2196 participants diagnosed with psychiatric illness, and 1115 (50.8%) of them were males, were included in our data. Six studies were cross-sectional [11, 12, 16, 20, 22, 23], five were case-controls [10, 13, 14, 15, 17], two were prospective cohorts [9, 18], and two were retrospective cohorts [19, 21]. Three studies were conducted in Italy [9, 20, 21], two in the Netherlands [11, 22], one in France [10], one in Greece [12], one in Germany [13], one in Turkey [14], one in China [15], one in Lebanon [16], one in Egypt [17], one in Finland [18], one in Korea [19], and one in Serbia [23]. The earliest study was conducted in 2016 [22] and the latest in 2024 [15].

Clinical outcomes

Four studies included patients with AD [9-12], three included patients with bipolar disorder [13-15], two included patients with Schizophrenia [16, 17], and the rest included multiple psychiatric disorders [18-23]. Fourteen studies used chemiluminescence Immunoassay (CLIA) to assess vitamin D levels [9-22] and only one used high-performance liquid chromatography [23]. However, multiple scales were used to assess the psychiatric features. The prevalence of vitamin D deficiency among patients with mental illnesses ranged from 22% in schizophrenia patients [17] to 76% in AD patients [11].

Regarding multiple mental illnesses, vitamin D deficiency is significantly associated with hypoperfusion in brain areas [19] and the acute phase of mental relapses [20]. In AD patients, vitamin D may be useful short- and long-term predictors of cognitive deterioration [9, 12], motoric cognitive risk [10], and depression [11]. In bipolar patients, a manic episode may be triggered by a decreased vitamin D level [14] and the worsening of depression [15]. Patients with first-episode schizophrenia should have their plasma vitamin D levels tested, particularly if they have a longer duration of untreated psychosis (410 weeks) and more pronounced negative and severe depressive symptoms [17].

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(6), 464-473 | ISSN:2251-6727

Table (1): The sociodemographic attributes of the participating populations.

Study	Study design	Country	Participants	Mean age/ range	Males (%)
Murdaca et al., 2021 [9]	Prospective cohort	Italy	118	86 ± 5	30 (25.4%)
Le Floch et al., 2022 [10]	Case-control	France	244	71.4 ± 3.7	145 (59.4%)
Richter et al., 2023 [11]	Cross-sectional	The Netherlands	25	81.2 ± 8	13 (52%)
Mavraki et al., 2020 [12]	Cross-sectional	Greece	138	75.5	71 (51.4%)
Leser et al., 2023 [13]	Case-control	Germany	86	45.17 ± 13.15	47 (54.7%)
İmre et al., 2023 [14]	Case-control	Turkey	34	37.8 ± 10.4	15 (44.1%)
Zheng et al., 2024 [15]	Case-control	China	149	29.2 ± 14.4	63 (42.3%)
Zoghbi et al., 2020 [16]	Cross-sectional	Lebanon	196	37.3 ± 11.7	118 (60.2%)
El Taweel et al., 2017 [17]	Case-control	Egypt	50	23.8	50 (100%)
Ikonen et al., 2019 [18]	Prospective cohort	Finland	328	27.9	152 (46.3%)
Sultana et al., 2022 [19]	Retrospective cohort	Korea	19	28.4 ± 9.2	3 (16%)
Fabrazzo et al., 2022 [20]	Cross-sectional	Italy	152	47.3 ± 14.4	75 (49.3%)
Cuomo et al., 2019 [21]	Retrospective cohort	Italy	290	47.8	127 (43.8%)
Boerman et al., 2016 [22]	Cross-sectional	The Netherlands	320	47	186 (58%)
Ristic et al., 2017 [23]	Cross-sectional	Serbia	47	45.6	20 (42.6%)

Table (2): Clinical features and results of the included research.

Study ID	Depression scale	Anxiety scale	Vitamin D level diagnosis	Prevalence of vitamin D deficiency	Conclusions	JBI
Murdaca et al., 2021 [9]	AD	MMSE	CLIA	NM	In AD patients, VD may be useful short- and long-term predictors of cognitive deterioration.	Moderate

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(6), 464-473 | ISSN:2251-6727

Le Floch et al., 2022 [10]	AD	MMSE	CLIA	59 (24.2%)	The motoric cognitive risk was linked to hypovitaminosis D in elderly community dwellers who were free of dementia.	Moderate
Richter et al., 2023 [11]	AD	the Middelheim Frontality Score (MFS), Behavioral Pathology in AD Rating Scale, and Cornell Scale for Depression in Dementia (CSDD)	CLIA	19 (76%)	Serum 5-HT levels were linked favorably with aggression, frontal behavior, depression, and somewhat cognitive function, while serum 25(OH)D3 concentrations correlated inversely with CSF amyloid-beta (Aβ1-42).	Moderate
Mavraki et al., 2020 [12]	AD	MMSE	CLIA	62 (44.9%)	Patients with AD disease and participants with mild cognitive impairment have considerably lower serum vitamin D levels.	Moderate
Leser et al., 2023 [13]	Bipolar disorder	the Trail Making Test Part A/B, the Color-Word Interference Test, and the California Verbal Learning Test (CVLT)	CLIA	35 (40.7%)	In euthymic bipolar patients, the current study does not support vitamin D metabolism as a modifying factor of cognitive performance.	High
İmre et al., 2023 [14]	Bipolar disorder	Depression Rating Scale (HAM-D) and Young Mania Rating Scale (YMRS)	CLIA	19 (55.8%)	A manic episode may be triggered by a decreased vitamin D level; a vitamin D shortage may result from inadequate sunlight exposure or malnourishment during the manic phase.	Moderate
Zheng et al., 2024 [15]	Bipolar disorder	the Zung Self-Rating Depression Scale (SDS)	CLIA	93 (62.4%)	When compared to a medium-level profile, there was a significant nonlinear link (P for trend <0.05) between the improvement in depression and the vitamin D high-level profile.	Moderate
Zoghbi et al., 2020 [16]	Schizophrenia	BCRS and MRSS	CLIA	111 (56.6%)	After controlling for variables, there was a significant correlation identified between	Moderate

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(6), 464-473 | ISSN:2251-6727

					severe VD insufficiency and a rise in the Morningside Rehabilitation Status Scale (MRSS) score and no significant correlation with the score on the Brief Cognitive Rating Scale (BCRS).	
El Taweel et al., 2017 [17]	Schizophrenia	The MADRS	CLIA	11 (22%)	When compared to healthy controls, serum 25(OH)D levels were lower in patients with schizophrenia. Patients with first-episode schizophrenia should have their plasma 25(OH)D levels tested, particularly if they have a longer duration of untreated psychosis (410 weeks) and more pronounced negative and severe depressive symptoms.	Moderate
Ikonen et al., 2019 [18]	Schizophrenia, psychosis, and non-psychotic depression	A questionnaire	CLIA	161 (49.1%)	Vitamin D scores in the outpatient population do not differ between the groups with schizophrenia, other psychoses, non-psychotic depression, and controls.	Moderate
Sultana et al., 2022 [19]	Neuropsychiatric lupus	MMSE	CLIA	12 (63.2%)	There is a noteworthy positive connection ($p<0.05$) between the level of vitamin D and hypoperfusion in brain areas associated with cognitive performance.	Moderate
Fabrazzo et al., 2022 [20]	Psychosis	Brief Psychiatric Rating Scale (BPRS)	CLIA	NM	Lower serum levels of PTH and 25-OH-Vit D may have a different correlation with the acute phase of mental relapses than with psychiatric outpatients who have reached pharmacological and psychopathological stabilization.	Moderate
Cuomo et al., 2019 [21]	Patients with mental illness	NM	CLIA	89 (30.7%)	Vitamin D levels have no correlation with psychiatric drugs ($p = 0.935$).	Moderate
Boerman et al., 2016 [22]	Bipolar disorder, schizophrenia, or schizoaffective disorder	DSM-IV	CLIA	97 (30.3%)	Outpatients with bipolar disorder, schizophrenia, or schizoaffective disorder had a 4.7-fold higher prevalence of	Moderate

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(6), 464-473 | ISSN:2251-6727

					vitamin D deficiency. Outpatients with bipolar disorder, schizophrenia, or schizoaffective disorder should be thought of as potentially at risk for low vitamin D levels due to the high prevalence of vitamin D insufficiency.	
Ristic et al., 2017 [23]	Schizophrenia, mood disorders, and other disorders	MMSE	HPLC	32 (68%)	It was much more common than anticipated for people with mental illnesses to be vitamin D deficient. A further link between the deficit and several electrolyte homeostasis problems was found.	High

*NM=Not-mentioned

Discussion

This comprehensive review investigated the association between vitamin D levels the progression of mental illnesses and the associated psychological features. The highest prevalence of hypovitaminosis D was found among AD patients (76%) [11]. We found that in AD patients, vitamin D may be useful short- and long-term predictors of cognitive deterioration [9, 12], motoric cognitive risk [10], and depression [11]. **Annweiler *et al.*** reported that Serum vitamin D concentrations were lower in AD individuals than in matched controls. This supports the idea that vitamin D is a "neurosteroid hormone" and that it may be a biomarker for AD [24]. **Pinzon *et al.*** also presented evidence of the link between low vitamin D levels and the risk of AD. According to the random effects model study, having low vitamin D levels (less than 25 ng/ml) increases the chance of getting AD [25].

There are two possible neuropathology changes that contribute to the pathomechanism of AD. A positive lesion resulting from the buildup of amyloid plaques, neurofibrillary tangles, and other deposits in the brain of an AD patient is the initial neuropathology alteration. The loss of neuropil, neuronal, and synaptic, is the cause of the second alteration in neuropathology. Furthermore, oxidative stress and neuroinflammation are two more variables that might lead to neurodegeneration [26]. Numerous studies have documented the possible advantages of vitamin D and its connection to AD. Studies on humans and animals have shown that vitamin D may influence the initial neuropathology alteration by encouraging the removal of amyloid plaques [27]. Although its exact mechanism is yet unknown, vitamin D also prevents cognitive impairment through its functions in neuroprotection, neurotrophy, neurotransmission, and neuroplasticity [28]. In in vitro experiments, vitamin D also demonstrated the ability to reduce neuroinflammation by blocking the synthesis of TNF-a and IL 6 [29].

This study found that in bipolar patients, a manic episode may be triggered by a decreased vitamin D level [14] and the worsening of depression [15]. Extensive research on vitamin D deficiency in individuals experiencing depression has been published in the literature, with findings indicating that the pathophysiology of depression is significantly impacted by vitamin D deficiency [30, 31]. Still, not enough research has been done on the potential connection between vitamin D and manic episodes.

Because it keeps the equilibrium between pro- and anti-inflammatory processes, vitamin D is known as a neuromodulator molecule [32]. The active form of vitamin D, 1,25-dihydroxy vitamin D3, has been shown to have anti-inflammatory properties, and a shortage of it can exacerbate inflammatory processes [33]. Vitamin D3 is regulated by the enzymes tryptophan hydroxylase and tyrosine hydroxylase. The synthesis of serotonin, dopamine, norepinephrine, and epinephrine is rate-

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(6), 464-473 | ISSN:2251-6727

limited by these two enzymes. Furthermore, vitamin D inhibits the enzyme inducible nitric oxide synthase (iNOS) to produce antioxidant effects [34]. Through the previously indicated processes, vitamin D insufficiency may contribute to the genesis of psychiatric diseases, particularly bipolar manic episodes.

The current study found that patients with first-episode schizophrenia should have their plasma vitamin D levels tested, particularly if they have a longer duration of untreated psychosis (410 weeks) and more pronounced negative and severe depressive symptoms [17]. In a meta-analysis by **Zhu *et al.*,** schizophrenia was more common in those who were deficient in vitamin D [35]. Despite the fact that multiple epidemiological research have looked at the effect of vitamin D on schizophrenia, the results are inconsistent. As one study recorded the lowest prevalence of vitamin D deficiency (22%) [17] and the other recorded that over half of schizophrenic patients (56.6%) [16] had vitamin D deficiency.

It is currently unknown what processes vitamin D insufficiency may have in relation to schizophrenia. The fact that these individuals tend to spend less time outside could be the cause of their low vitamin D levels [36]. Some researchers think that there may be a connection between vitamin D and schizophrenia in the early stages of life. According to certain theories, schizophrenia may be predisposed by embryonic vitamin D insufficiency [37, 38]. The dopamine hypothesis of schizophrenia appears to be a plausible pathway in the pathology of schizophrenia, according to findings from animal models that indicate developmental vitamin D deficiency during the gestational period affects dopamine metabolism and modifies the dopamine system in the developing brain of rats [39, 40].

Some limitations of the current review are that just a portion of the neurodegenerative and psychiatric illnesses are considered, and it is not a systematic review. Notwithstanding these drawbacks, it makes clear that, according to the papers we looked at, there is no evidence to support vitamin D's function as a biomarker in these illnesses.

Conclusion

One of the vitamins that has been researched the most globally is vitamin D, and research on its biological function in humans is still quite interesting. Low vitamin D levels are found in neurological and psychiatric patients, but the significance of these findings is not entirely clear because low vitamin D levels are also frequently found in healthy subjects or because several study flaws severely reduce the significance of the findings. Future studies' primary objective would be to map out the variables affecting supplementing efficacy and identify people who benefit from taking vitamin D analogs. This may contribute to the advancement of vitamin D understanding in relation to practical therapeutic needs.

References:

1. Bikle, D.; Christakos, S. New aspects of vitamin D metabolism and action—Addressing the skin as source and target. Nat. Rev. Endocrinol. 2020, 16, 234–252.
2. Bivona G, Gambino CM, Lo Sasso B, Scazzone C, Giglio RV, Agnello L, Ciaccio M. Serum vitamin D as a biomarker in autoimmune, psychiatric and neurodegenerative diseases. Diagnostics. 2022 Jan 6;12(1):130.
3. Brown AJ, Slatopolsky E. Vitamin D analogs: therapeutic applications and mechanisms for selectivity. Molecular aspects of medicine. 2008 Dec 1;29(6):433-52.
4. Cohen-Lahav M, Shany S, Tobvin D, Chaimovitz C, Douvdevani A. Vitamin D decreases NFκB activity by increasing IκBα levels. Nephrology Dialysis Transplantation. 2006 Apr 1;21(4):889-97.
5. Máčová L, Bičíková M, Ostatníková D, Hill M, Stárka L. Vitamin D, neurosteroids and autism. Physiological research. 2017 Jun 3;66(4).
6. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. International journal of surgery. 2021 Apr 1;88:105906.
7. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. Systematic reviews. 2016 Dec;5:1-0.
8. Munn Z, Aromataris E, Tufanaru C, Stern C, Porritt K, Farrow J, Lockwood C, Stephenson

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(6), 464-473 | ISSN:2251-6727

M, Moola S, Lizarondo L, McArthur A. The development of software to support multiple systematic review types: the Joanna Briggs Institute System for the Unified Management, Assessment and Review of Information (JBI SUMARI). JBI evidence implementation. 2019 Mar 1;17(1):36-43.

9. Murdaca G, Banchero S, Tonacci A, Nencioni A, Monacelli F, Gangemi S. Vitamin D and folate as predictors of MMSE in Alzheimer's disease: a machine learning analysis. Diagnostics. 2021 May 24;11(6):940.
10. Le Floch M, Gautier J, Annweiler C. Vitamin D concentration and motoric cognitive risk in older adults: Results from the Gait and Alzheimer Interactions Tracking (GAIT) Cohort. International Journal of Environmental Research and Public Health. 2022 Oct 12;19(20):13086.
11. Richter AL, Diepeveen-de Bruin M, Balvers MG, De Groot LC, De Deyn PP, Engelborghs S, Witkamp RF, Vermeiren Y. Association between low vitamin D status, serotonin and clinico-bio-behavioral parameters in Alzheimer's disease. Dement Geriatr Cogn Disord. 2023 Oct 6;10:000534492.
12. Mavraki E, Ioannidis P, Tripsianis G, Gioka T, Kolousi M, Vadikolias K. Vitamin D in mild cognitive impairment and Alzheimer's disease. A study in older Greek adults. Hippokratia. 2020 Jul;24(3):120.
13. Leser B, Dalkner N, Tmava-Berisha A, Fellendorf FT, Unterrainer HF, Stross T, Maget A, Platzer M, Bengesser SA, Häussl A, Zwigl I. The Influence of Vitamin D Status on Cognitive Ability in Patients with Bipolar Disorder and Healthy Controls. Nutrients. 2023 Sep 22;15(19):4111.
14. İmre O, Karaağaç M, Caglayan C. Does Decreased Vitamin D Level Trigger Bipolar Manic Attacks?. Behavioral Sciences. 2023 Sep 18;13(9):779.
15. Zheng X, Neeraj D, Zhu Q, Zhang Y, Li T, Yang W, Guan N. Latent profile analysis of vitamin D and its association with depression severity of hospitalized patients with bipolar depression. Nutritional Neuroscience. 2024 May 24:1-9.
16. Zoghbi M, Haddad C, Hallit S, Nabout R, Medlej-Hashim M, Hachem D, Azar J. Cognition and physical functioning in patients with schizophrenia: any role for vitamin D?. Nutritional neuroscience. 2020 Nov 1;23(11):911-9.
17. El Taweel ME, El Shafei T. Relationship between vitamin D status and psychopathology in patients with first-episode schizophrenia: a cross-sectional study. Middle East Current Psychiatry. 2017 Jan 1;24(1):43-8.
18. Ikonen H, Palaniswamy S, Nordström T, Järvelin MR, Herzig KH, Jääskeläinen E, Seppälä J, Miettunen J, Sebert S. Vitamin D status and correlates of low vitamin D in schizophrenia, other psychoses and non-psychotic depression–The Northern Finland Birth Cohort 1966 study. Psychiatry research. 2019 Sep 1;279:186-94.
19. Sultana N, Sarkar AK, Matsuda H, Ihsan MA, Haq SA, Arefin MS, Islam SN. Relationship between vitamin D status and brain perfusion in neuropsychiatric lupus. Nuclear Medicine and Molecular Imaging. 2022 Jun;56(3):158-68.
20. Fabrazzo M, Agnese S, Cipolla S, Di Vincenzo M, Mancuso E, Volpicelli A, Perris F, Sampogna G, Catapano F, Fiorillo A, Luciano M. Vitamin D Deficiency and Risk Factors Related to Acute Psychiatric Relapses in Patients with Severe Mental Disorders: A Preliminary Study. Brain Sciences. 2022 Jul 24;12(8):973.
21. Cuomo A, Maina G, Bolognesi S, Rosso G, Beccarini Crescenzi B, Zanobini F, Goracci A, Facchi E, Favaretto E, Baldini I, Santucci A. Prevalence and correlates of vitamin D deficiency in a sample of 290 inpatients with mental illness. Frontiers in psychiatry. 2019 Mar 29;10:167.
22. Boerman R, Cohen D, Schulte PF, Nugter A. Prevalence of vitamin D deficiency in adult outpatients with bipolar disorder or schizophrenia. Journal of clinical psychopharmacology. 2016 Dec 1;36(6):588-92.
23. Ristic S, Kocic SS, Milovanovic DR, Mihajlovic G, Mihailovic N, Lucic AT,

Zivanovic S. Vitamin D status in patients with mental disorders: a cross-sectional analysis of single cohort from routine practice. Acta Endocrinologica (Bucharest). 2017 Jan;13(1):40.

24. Annweiler C, Llewellyn DJ, Beauchet O. Low serum vitamin D concentrations in Alzheimer's disease: a systematic review and meta-analysis. Journal of Alzheimer's Disease. 2013 Jan 1;33(3):659-74.
25. Pinzon RT, Handayani T, Wijaya VO, Buana RB. Low vitamin D serum levels as risk factor of Alzheimer's disease: a systematic review and meta-analysis. The Egyptian Journal of Neurology, Psychiatry and Neurosurgery. 2023 Jul 3;59(1):88.
26. Breijyeh Z, Karaman R. Comprehensive review on Alzheimer's disease: causes and treatment. Molecules. 2020;25(24):5789.
27. Briones TL, Darwish H. Vitamin D mitigates age-related cognitive decline through the modulation of pro-inflammatory state and decrease in amyloid burden. J Neuroinflammation. 2012;9:244.
28. Anjum I, Jaffery SS, Fayyaz M, Samoo Z, Anjum S. The role of vitamin D in brain health: a mini literature review. Cureus. 2018.
29. Lefebvre d'Hellencourt C, Montero-Menei CN, Bernard R, Couez D. Vitamin D3 inhibits proinflammatory cytokines and nitric oxide production by the EOC13 microglial cell line. J Neurosci Res. 2003;71(4):575–82.
30. Patrick, R.P.; Ames, B.N. Vitamin D and the omega-3 fatty acids control serotonin synthesis and action, part 2: Relevance for ADHD, bipolar disorder, schizophrenia, and impulsive behavior. FASEB J. 2015, 29, 2207–2222.
31. Stumpf,W.E.; Privette, T.H. Light, vitamin D and psychiatry. Psychopharmacology 1989, 97, 285–294.
32. Sassi, F.; Tamone, C.; D'Amelio, P. Vitamin D: Nutrient, Hormone, and Immunomodulator. Nutrients 2018, 10, 1656.
33. Ao, T.; Kikuta, J.; Ishii, M. The Effects of Vitamin D on Immune System and Inflammatory Diseases. Biomolecules 2021, 11, 1624.
34. Garcion, E.; Sindji, L.; Montero-Menei, C.; Andre, C.; Brachet, P.; Darcy, F. Expression of inducible nitric oxide synthase during rat brain inflammation: Regulation by 1,25-dihydroxyvitamin D3. Glia 1998, 22, 282–294.
35. Zhu JL, Luo WW, Cheng X, Li Y, Zhang QZ, Peng WX. Vitamin D deficiency and schizophrenia in adults: a systematic review and meta-analysis of observational studies. Psychiatry research. 2020 Jun 1;288:112959.
36. McGrath JJ, Burne TH, Feron F, Mackay-Sim A, Eyles DW. Developmental vitamin D deficiency and risk of schizophrenia: a 10-year update. Schizophr Bull. 2010;36(6):1073–1078.
37. McGrath JJ, Eyles DW, Pedersen CB, et al. . Neonatal vitamin D status and risk of schizophrenia: a population-based case-control study. Arch Gen Psychiatry. 2010;67(9):889–894.
38. Kesby JP, Eyles DW, Burne TH, McGrath JJ. The effects of vitamin D on brain development and adult brain function. Mol Cell Endocrinol. 2011;347(1–2):121–127.
39. Kesby JP, Cui X, Burne TH, Eyles DW. Altered dopamine ontogeny in the developmentally vitamin D deficient rat and its relevance to schizophrenia. Front Cell Neurosci. 2013;7:111.
40. Howes OD, Kapur S. The dopamine hypothesis of schizophrenia: version iii—the final common pathway. Schizophr Bull. 2009;35(3):549–562.