



DEMENTIA AND THE SUNSHINE VITAMIN ASSOCIATION – A SYSTEMATIC LITERATURE REVIEW

Geriatric Health

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ABSTRACT

WHO recognizes dementia as a public health priority. Dementia is a syndrome in which there is deterioration in cognitive function. Vitamin D obtained from sun exposure, foods, and supplements is the sunshine vitamin recognized for bone health. So far focus has been only on bone health and Vit D Hypovitaminosis D, or deficiency in vitamin D, has been linked to an increased risk of developing dementia and Alzheimer's disease. A systematic literature review was done with data base study and 23 studies were selected with total of 36875 adult mainly elder age group participants. Out of those 9 were not showing association of Vit D and cognitive decline. The remaining 14 studies had association between vit D and cognitive decline. There are variables confounding the results and there need to be more studies and research on brain function and factors affecting brain health. This is a pressing concern and timely supplementation of Vit D if proven could help make Alzheimer and dementia preventable.

KEYWORDS

dementia, Alzheimer, Vit D, 25(OH)D, cognitive decline, hypovitaminosis, Vit D deficiency

INTRODUCTION

Dementia is a syndrome in which there is deterioration in cognitive function beyond what might be expected from the usual consequences of biological ageing, of ageing. Currently more than 55 million people live with dementia worldwide, and there are nearly 10 million new cases every year, and it is a major cause of disability and dependency in older people globally. Alzheimer's disease is the most common form of dementia and may contribute to 60-70% of cases.¹

WHO recognizes dementia as a public health priority. In May 2017, the World Health Assembly endorsed the Global action plan on the public health response to dementia 2017-2025. The Plan provides a comprehensive blueprint for action – for policy-makers, international, regional and national partners, and WHO as in the following areas: addressing dementia as a public health priority; increasing awareness of dementia and creating a dementia-inclusive society; reducing the risk of dementia; diagnosis, treatment and care; information systems for dementia; support for dementia carers; and, research and innovation.

WHO's Guidelines on risk reduction of cognitive decline and dementia provide evidence-based recommendations on interventions for reducing modifiable risk factors for dementia, such as physical inactivity and unhealthy diets, as well as controlling medical conditions linked to dementia, including hypertension and diabetes.

Vitamin D (also referred to as “calciferol”) is a fat-soluble vitamin that is naturally present in a few foods, added to others, and available as a dietary supplement. It is also produced endogenously when ultraviolet (UV) rays from sunlight strike the skin and trigger vitamin D synthesis.⁽²⁾

Intake reference values for vitamin D and other nutrients are provided in the Dietary Reference Intakes (DRIs) developed by the Food and Nutrition Board (FNB) at the Institute of Medicine of The National Academies (formerly National Academy of Sciences). DRI is the general term for a set of reference values used to plan and assess nutrient intakes of healthy people.⁽³⁾ These values, which vary by age and gender, include:

Recommended Dietary Allowance (RDA): average daily level of intake sufficient to meet the nutrient requirements of nearly all (97%–98%) healthy people.

Adequate Intake (AI): established when evidence is insufficient to develop an RDA and is set at a level assumed to ensure nutritional adequacy.

Tolerable Upper Intake Level (UL): maximum daily intake unlikely to cause adverse health effects.

The FNB established an RDA for vitamin D representing a daily intake

that is sufficient to maintain bone health and normal calcium metabolism in healthy people. RDAs for vitamin D are listed in both International Units (IUs) and micrograms (mcg); the biological activity of 40 IU is equal to 1 mcg (Table 1). Even though sunlight may be a major source of vitamin D for some, the vitamin D RDAs are set on the basis of minimal sun exposure.⁽⁴⁾

Vitamin D obtained from sun exposure, foods, and supplements vitamin D promotes calcium absorption in the gut and maintains adequate serum calcium and phosphate concentrations to enable normal bone mineralization. Vitamin D has other roles in the body, including reduction of inflammation as well as modulation of such processes as cell growth, neuromuscular and immune function, and glucose metabolism [4-7]. Vitamin D and Health.

The FNB committee that established DRIs for vitamin D found that the evidence was inadequate or too contradictory to conclude that the vitamin had any effect on a long list of potential health outcomes (e.g., on resistance to chronic diseases or functional measures), except for measures related to bone health. However, research has been conducted on vitamin D and numerous health outcomes are being evaluated for association with Vit D: bone health and osteoporosis, cancer, cardiovascular disease (CVD), depression, multiple sclerosis (MS), type 2 diabetes, and weight loss⁽³⁾

Table 1: Recommended Dietary Allowances (RDAs) for Vitamin D [1]

Age	Male	Female	Pregnancy	Lactation
0-12 months*	10 mcg (400 IU)	10 mcg (400 IU)		
1-13 years	15 mcg (600 IU)	15 mcg (600 IU)		
14-18 years	15 mcg (600 IU)	15 mcg (600 IU)	15 mcg (600 IU)	15 mcg (600 IU)
19-50 years	15 mcg (600 IU)	15 mcg (600 IU)	15 mcg (600 IU)	15 mcg (600 IU)
51-70 years	15 mcg (600 IU)	15 mcg (600 IU)		
>70 years	20 mcg (800 IU)	20 mcg (800 IU)		

Source. <https://ods.od.nih.gov/factsheets/VitaminD-HealthProfessional/#h2>

Hypovitaminosis D, or deficiency in vitamin D, has been linked to an increased risk of developing dementia and Alzheimer's disease. A 2021 meta-analysis of 16 studies found that low vitamin D levels were significantly associated with an increased risk of cognitive impairment and Alzheimer's disease, particularly in those over the age of 65 (8). Another study published in 2021 examined the potential mechanisms underlying this relationship and found that vitamin D deficiency may contribute to the development of Alzheimer's disease through its

effects on amyloid-beta and tau proteins(9).

There are dearth of studies which show no impact of Vit D on cognition or other diseases also In a study late middle age white and black participants did not find significant associations between lower levels of 25(OH)D with lower cognitive test scores at baseline, change in scores over time or dementia risk. (5)

A systematic literature review was done to evaluate the studies presenting findings on vit d and cognitive decline as there is no definite guideline on its role in cognition or brain health.

METHODOLOGY

The databases Pubmed ,Google scholar ,science direct and web of science were searched for English-language studies up to Feb 2023. Two authors independently extracted data and assessed study quality using predefined criteria. There were 189 studies with inclusion criteria -elderly population, RCT or observational study ,over last 20 years .There was final selection of 23 studies which were analyzed for association between Vit D and Cognitive decline.

RESULTS

S no	Name ,	Author	Type & Year	Number	intervention	Results
1	Effect of Long-term Vitamin D3 Supplementation vs Placebo on Risk of Depression or Clinically Relevant Depressive Symptoms and on Change in Mood Scores	Olivia I. Okereke et al	RCT	18 353 Adults 50 yrs & older	Treatment with VitD & Placebo	These findings do not support the use of vitamin D3 in adults to prevent depression.
2	Can vitamin D supplementation prevent winter-time blues? J C Dumville	J C Dumville et al	RCT	2117 older women over 70 yrs	with 800 IU of vitamin D daily	did not lead to an improvement in mental health scores.
3	Vitamin D supplementation for treatment of seasonal affective symptoms in healthcare professionals:	Tenna Bloch Frandsen Et al	a double-blind RCT	and 34 healthcare personnel	daily dose of 70 µg vitamin D or placebo	study failed to demonstrate an effect of vitamin D on SAD symptoms, but our findings may be limited by confounders
4	Annual high-dose vitamin D3 and mental well-being:	Kerrie M Sanders et al	RCT 2011	2317 women between 2003 and 2005 women aged 70 or older	500 000 IU vitamin D(3) (cholecalciferol) orally or placebo 3 months for 3 years	does not support the hypothesis that an annual high dose of vitamin D(3) as intervention to prevent depressive symptoms
5	**Vitamin D supplementation for the prevention of depression and poor physical function in older persons: the D-Vitaal study,	Elisa J de Koning	RCT	155 age60-80	1200 IU/d vitamin D3 (n = 77) or placebo tablets (n = 78)	no effect on depressive symptoms and physical functioning in older persons with relatively
6	No improvement in depressive symptoms by vitamin D supplementation: results from a randomised controlled trial	Rolf Jorde	RCT 408 age51-4 and 52-5 years	the 408	20 000 IU (500 µg) per week randomised	we have not been able to demonstrate any significant effect of vitamin D supplementation 8on depressive symptoms.
7	Effect of vitamin D supplementation on depressive symptoms and psychological wellbeing in healthy adult women	Maria A.	RCT healthy women (18–40 years	152	randomly assigned to receive 50 000 IU (1·25 mg) of oral vitamin D3 or placebo once per month for 6 months	We found no evidence of any beneficial effect of monthly vitamin D3 supplementation on mood-related outcomes in healthy premenopausal women over the winter period
8	. Effects of vitamin D supplementation on symptoms of depression in overweight and obese subjects: randomized double blind trial. J Intern Med 264, 599-609	Jorde R, Sneve M, Figenschau Y, Svartberg J, Waterloo K	Cross-sectional study and RCT	A total of 441 subjects aged 21-70 years	of 20,000 or 40,000 IU vitamin D per week versus placebo for 1 year.	It appears to be a relation between serum levels of 25(OH)D and symptoms of depression. Supplementation with high doses of vitamin D seems to ameliorate these symptoms indicating a possible causal relationship.
10	Vit D status cognitive decline and incident dementia -the Canadian study of health and ageing	C.Duchaine et al	Cohort study	(2020) 661 Age 65 years or older total of 661	10-year cohort study of a representative sample of individuals aged 65 years or older associations of plasma 25-hydroxyvitamin D.	This study does not support a protective effect of vitamin D status on cognitive function
111	Brain vitamin D forms, cognitive decline, and neuropathology in community-dwelling older adults	M. Shea, K. Barger, +10 authors S. Booth	December 2022	n = 290	vitamin D concentrations measured in four brain regions	Higher brain 25(OH)D3 concentrations were associated with better cognitive function prior to death
12	Vitamin D Status and Rates of Cognitive Decline in a Multiethnic Cohort of Older Adults.	Joshua W. Miller, D. Harvey	Longitudinal multiethnic cohort	N=382	Yearly follow up Vit de levels baseline and FU cognitive assessment	Low VitD status was associated with accelerated decline in cognitive function domains in ethnically diverse older adults, including African American and Hispanic individuals who exhibited a high prevalence of VitD insufficiency or deficiency.

13	DOI:10.1210/jc.2017-02462**Vitamin D Status and Intakes and Their Association With Cognitive Trajectory	M. Beydoun, S. Hossain	Longitudinal Study of Urban Adults	1231 to 1803 (30-64yrs) of 4.64 ± 0.93 years (30 to 64 years	FU of Cognitive performance trajectory over visits with dietary or supplementary intake vit D	Vitamin D status and intakes were inversely related to domain-specific cognitive decline in US urban adults.
14	Low 25-Hydroxyvitamin D Concentrations and Risk of Incident Cognitive Impairment in Black and White Older Adults: The Health ABC Study	Laurel B Kilpatrick, D. Houston	CS	2,786	Measurement of cognitive impairment and 25(OH)D concentrations	. In whites, 25(OH)D concentrations <30ng/mL were not associated with prevalent or incident cognitive impairment. Black participants with 25(OH)D concentrations <20ng/mL had a higher odds of prevalent, but not incident cognitive impairment Low 25(OH)D concentrations were associated with twofold higher odds of prevalent cognitive impairment in blacks
15	**association of vitamin d with mild cognitive impairment and alzheimer's dementia in older mexican adults.	S. Aguilar-Navarro	Cross sectional study	208 Age 70 yrs and older	evaluated subjects with MCI, AD, and normal cognition (NC) with available serum Vitamin D [25(OH)D] levels (past 6 months	Serum Vitamin D deficiency was associated with MCI and dementia; low levels produced a greater effect over executive functions.
16	Association of vitamin D metabolites with cognitive function and brain atrophy in elderly individuals - the Austrian stroke prevention study	S. Zelzer	Cross sectional	390	25(OH)D3, 25(OH)D2 and 24,25(OH)2D3 were measured All participants underwent thorough neuropsychiatric tests	Vitamin D deficient individuals appear to have a modest reduction of memory function without structural brain atrophy. Future studies should explore if vitamin D supplementation can improve cognitive function .
17	Vitamin D and the risk of dementia and Alzheimer disease	T. Littlejohns	2014/ CS	1658 adults	Cognitive assessment and 25(OH)D] levels	confirm that vitamin D deficiency is associated with a substantially increased risk of all-cause dementia and Alzheimer disease
18	Association between vitamin D receptor gene polymorphism and Alzheimer's disease.	D. Gezen-Ak et al -	2007 CS	213	Apal genotypes for Vit D receptor gene testing in AD patients	this study provides evidence for a possible link between AD and vitamin D
20	Serum Vitamin D Concentrations and Cognitive Function in a Population-Based Study among Older Adults in South Germany.	G. Nagel,et al	2010 CS study	1373/ 65 yr above	the cognitive performance assessment and serum 25(OH)D levels measured	Our results suggest an association between vitamin D deficiency and cognitive function in specific domains in community dwelling older adults.
21	Serum 25-hydroxyvitamin D predicts cognitive performance in adults	H. Darwish,et al	2015 cross sect study	254 adults older -60 yrs above and younger 30-60 yrs	the cognitive performance assessment and serum 25(OH)D levels measured	These findings suggest that correction of vitamin D needs to be explored as an intervention to prevent cognitive impairment
22	**The Association of Vitamin D Status with Mild Cognitive Impairment and Dementia Subtypes: A Cross-Sectional Analysis in Dutch Geriatric Outpatients.	A. Janse et al	A Cross-Sectional Analysis 2023	1,758	Measured Vit D levels in patients with mild cognitive impairment and dementia	did not find differences in 25(OH)D levels of mild cognitive impairment (MCI) or other dementia patients compared to ND patients, nor differences in comparing dementia subtypes
23	25-Hydroxyvitamin D levels and cognitive performance and decline in elderly men	Y. Slinin/	cohort 2010	1,604	measured vit d levels ostoporotic 25(OH)D 4.6 yrs	Higher levels of plasma vitamin D in women aged 60–70 years were associated with better cognitive function about a decade later but were not associated with cognitive decline during 6 years of follow-up
24	Higher vitamin D dietary intake is associated with lower risk of alzheimer's disease: a 7-year follow-up.	C. Annweiler	2012 CS	498 women aged 75 years &older.	Measured Vit D levels and 7 year follow up patients with alzheimers	Higher vitamin D dietary intake was associated with a lower risk of developing AD among older women

There were total of 23 studies There were 36875 participants in the studies included in total .There were (RCT studies and the rest were cross sectional studies with 2 cohort studies.9 studies found no correlation between Vit D and cognition decline /The remaining 14 studies found a positive correlation between levels of Vit D and cognition decline., Seeing the number of patients with dementia it is worthwhile to do more research to implement health education and supplementation efforts for help prevent cognition decline in seniors.

DISCUSSION

There is a lot of research on the effects of Vit D on disease other than bone health .Dementia and Alzheimer's are increasing and causing death and disability .There is evidence suggesting a significant association between vitamin D deficiency and dementia. Low levels of serum 25-hydroxyvitamin D [25(OH)D], a stable marker of vitamin D status, have been linked to increased odds of prevalent cognitive dysfunction, Alzheimer's disease, and all-cause dementia in a number

of studies [11][12][13]. The risk of cognitive impairment was up to four times greater in severely deficient elders (25 (OH)D 25 nmol/L) compared to individuals with adequate levels (≥ 75 nmol/L)[12].(13)

Low levels of serum 25-hydroxyvitamin D [25 (OH)D], a stable marker of vitamin D status, are also associated with increased odds of prevalent cognitive dysfunction, Alzheimer's disease and all-cause dementia in a number of studies, raising the possibility that vitamin D plays a role in the etiology of cognitive dysfunction and dementia] "Associations have been noted between low 25-hydroxyvitamin D [25 (OH)D] and Alzheimers disease and dementia in both Europe and the US. Similarly, the risk of cognitive impairment was up to four times greater in the severely deficient elders (25 (OH)D 25 nmol/L) in comparison with individuals with adequate levels (≥ 75 nmol/L)(13) In the present literature review there are mixed findings with 9 studies not finding association between the Vit D levels and cognitive decline The differing findings lead to no consensus One potential explanation for these mixed findings is that the relationship between vitamin D and cognition may depend on other factors, such as age, sex, and the presence of other health conditions

Despite studies regarding Vit D role in cognition there is still an unmet need more focused research and public awareness and action to take steps for prevention from the effects of hypovitaminosis Vit D

CONCLUSIONS

There are studies with varying results but there are lot of confounding variables affecting the studies ,But overall there was a strong association with low Vit D levels and cognitive decline .There were 15 studies which indicated the need for a proactive approach to Vit D supplementation ,patient education ,identifying population at risk and ensuring nutritional deficiency of Vit D is not cause of disabling dementia.

Overall, these studies suggest that maintaining adequate vitamin D levels may be important in preventing cognitive decline and reducing the risk of developing dementia and Alzheimer's disease .Vit D supplementation for cognition should be researched more and appropriate steps taken for preventive cognition decline . There are variables confounding the results and there need to be more studies .and research on brain function and factors affecting brain health.This is a pressing concern and timely supplementation of Vit D if proven could help make Alzheimer and dementia preventable.

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