



## Vitamin D deficiency and psychological disorders

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### Abstract

The studies showed that, Vitamin D is involved in numerous brain processes, regulation of neurotrophic factors, neuroprotection, neuroplasticity and brain development. Vitamin D is crucial not only for bone health but for proper brain development and psychological functioning. However, low levels of vitamin D are associated with depression, schizophrenia and also seasonal affective disorder in adults, but there is conflicting evidence about the relationship between vitamin D deficiency and psychological disorders. Our analysis are consistent with the hypothesis that low vitamin D concentration is associated with psychological disorders, therefore in this review article, PubMed and Web of Science databases were searched from 2000 through 2014. Based on these publications, although our study did not address the issue as to whether the observed differences represent a causal relationship between vitamin D deficiency and psychiatric symptoms, the results are nonetheless important given the significance of vitamin D to overall health. We suggest that increased attention should be given to vitamin D deficiency in psychiatric disorders.

**Keywords:** Vitamin D, Deficiency, Psychological disorders

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### Introduction

Vitamin D (D represents D<sub>2</sub>, D<sub>3</sub>, or both), known as the “sunshine vitamin,” is necessary for essential biological functions such as bone and mineral metabolism, muscle function, psychological function and immunity. It is a secosterol produced endogenously in the skin from sun exposure or obtained from foods. One of the major physiologic functions of vitamin D is to maintain serum calcium and phosphorus levels in a healthy physiologic range to maintain a variety of metabolic functions, bone metabolism and transcription regulation (1,2).

Studies showed that, vitamin D deficiency is a common health problem in both developed and developing countries. It is postulated that one billion people worldwide have vitamin D deficiency or insufficiency due to reduced sun exposure or inadequate intake for various reasons. Its status is very different among various countries, which is due to the difference in many factors including sunlight exposure, dietary intake of vitamin D, and air pollution (1,2). Iran is a country with high prevalence of moderate to severe vitamin D deficiency (3-6). Vitamin D is a steroid hormone and mainly obtained from exposure to sunlight, food and dietary

supplements (7) and plays several important physiologic and psychological roles and associated with an increased risk of multiple sclerosis, hypertension, type I diabetes, cardiovascular heart disease, rheumatoid arthritis and many common deadly cancers (8,9).

It involved in numerous brain processes including neuroprotection, regulation of neurotrophic factors, neuroplasticity, brain development and neuroimmunomodulation (10).

### Factors affect vitamin D status

Several factors, can affect vitamin D status, include genetic factors, adiposity and factors affecting the cutaneous synthesis of vitamin D such as skin pigmentation and ethnicity, age, season and latitude, clothing that results in lack of skin exposure to the sun and use of sunscreens. Many studies argued that there is an essential factor associated with chronic health conditions, including mental health (11-13). Whereas others have shown no relationship and insufficient evidence for an association between vitamin D and mental health (14-16).

The importance of vitamin D effects on central nervous system (CNS) in both healthy and psychiatric populations

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### ■ Implication for health policy/practice/research/medical education

Vitamin D, known as the “sunshine vitamin,” is necessary for essential biological functions. Vitamin D is an essential nutrient that contributes to strong bones health and helps to control the amount of calcium in the blood. Many people have vitamin D deficiency or insufficiency due to reduced sun exposure or inadequate intake for various reasons. Recent evidence suggests that it may play a causative role in mental illness and also help in the prevention of many diseases and adequate levels of vitamin D are also associated with health benefits such as psychological function. Many studies show that the risk of psychological disorders is higher in patients with vitamin D deficiency. This paper is about the relationship between vitamin D deficiency and psychiatric disorders.

is less well appreciated and is vastly understudied compared to its known impact on health. Vitamin D receptors are present throughout the brain, and vitamin D deficiency is correlated with negative CNS effects in animal and human studies (17).

Low serum levels of vitamin D have been linked with mental health issues and is involved in numerous brain processes including neuroimmunomodulation, regulation of neurotrophic factors, neuroprotection, neuroplasticity and brain development (8,10) and might be associated with some psychological disorders and play an important role in the treatment of psychological disorders (14,15,18,19). Various cross-sectional studies have detected an association between vitamin D deficiency and depression and cognitive performance (11,12,20-22).

Our analysis is consistent with the hypothesis that level of vitamin D is associated with psychological disorders. Therefore in this article, PubMed and Web of Science databases were searched from 2000 through 2014 relating to vitamin D with psychological disorders as affective disorder, anxiety disorder, cognitive disorders and psychosis disturbance.

### Vitamin D deficiency and psychological disorders

Vitamin D deficiency is a common underdiagnosed condition that has received increasing attention in the world. Recent evidence from hundreds of studies has suggested that vitamin D is important for reducing the risk of a variety of chronic illnesses as mental disorders. Anglin *et al.* (23), in a systematic review identified one case-control study, ten cross-sectional investigations and three cohort studies investigating the association between depression and vitamin D deficiency, but no randomized controlled trial. Some studies also reported an association between vitamin D deficiency and cognitive impairment (24-26).

Eskandari *et al.* (27) showed that low vitamin D levels

were found to correlate with major depression. Mozaffari-Khosravi *et al.* (28) showed a statistically significant difference in mean of Beck Depression Inventory II test score between G300 and NTG ( $p= 0.003$ ). The results of the study revealed that first, the correction of vitamin D deficiency corrected the depression state. Secondly, a single injection dose of 300,000 IU of vitamin D was safe and further effective than a 150,000-IU dose.

Several animal knock-out models show increased vitamin D receptor associated with anxiety, decreased activity, and muscular and motor impairments, resembling phenotypic models and activating PKC and map PK pathways (29-32). The other studies also reported vitamin D deficiency and the presence of psychosis in adolescents (32-35).

Various investigations found that individuals with schizophrenia had significantly lower levels of vitamin D in the blood compared to the control groups (36).

However, some studies have failed to find a significant association (37) and some others have found that higher vitamin D concentrations are associated with increased risk of schizophrenia (6). In addition, data on the relationship between sunlight exposure and schizophrenia did not provide convincing support for the link (38).

Vitamin D deficiency and insufficiency are both highly prevalent in adolescents with severe mental illness. The preliminary relations between vitamin D deficiency and presence of psychotic features warrant further investigation as to whether vitamin D deficiency is a mediator of illness intensity, result of illness intensity, or both. Higher popularity of vitamin D deficiency but no greater risk of psychosis in African Americans, if established, may have special implications for health disparity and treatment outcome research (39). McGrath *et al.*, (35) in a cohort of Finnish children who received supplemental vitamin D in their first year of life had a lower risk of developing schizophrenia. However, the implication of this association is unclear because it was unrelated to adherence to vitamin D supplementation, was only obvious in males, and was not found with any other mental illness. Jorde *et al.* (40) in a research to examine the effect of vitamin D on depression, obese and overweight patients were randomized to receive 20,000 or 40,000 IU of vitamin D pills or placebo weekly for one year. At baseline, those with 25(OH) D concentrations lower than 16 ng/ml had greater beck depression inventory scores, demonstrating that they were further depressed, than those with higher 25(OH)D levels. The two groups receiving vitamin D supplementation had significant improvement in their scores, whereas the placebo group did not.

Vitamin D deficiency is common and frequently unrecognized and yet may be an important contributor to psychiatric illnesses so we should not leave this serious issue unresolved.

This review took place from March 2000 to March 2014. Although our review study, did not address the issue as

to whether the observed differences represent a causal relationship between vitamin D deficiency and psychiatric symptoms, the results are however important given the significance of vitamin D to overall health. Despite the mounting scientific evidence that vitamin D sufficiency is required for optimal health, concluded in a recent meta-analysis that low vitamin D concentration is associated with depression, however, further randomized controlled trials of vitamin D are needed to determine whether this association is causal. There have been a few randomized controlled trials studying the effects of vitamin D on depressive symptoms, but the findings are inconsistent (10,16,17). A recently published recent controlled trials did investigate the effects of vitamin D supplementation as adjuvant treatment in patients with major depressive disorder. The results revealed a significant improvement in patients being treated with an antidepressant and vitamin D as compared with patients receiving an antidepressant and placebo.

Psycho-geriatric patients may be at risk for vitamin D deficiency due to their age, dietary factors and less exposure to sunlight. However, there is inadequate knowledge regarding the actual vitamin D status in this group of patients. Hence, one aim of this study was to compare the level of vitamin D in a sample of psycho-geriatric patients with the level in the general population from the same area. Additionally, the study aimed to examine whether patients with depression differ from patients with other psychiatric diagnoses with regard to vitamin D status (4-9). We suggested, to explore its association with major mental illnesses by conducting large cross sectional studies. Randomized placebo controlled trial would also be needed to establish causation between vitamin D deficiency and psychological illnesses.

The studies showed that, vitamin D plays a role in numerous brain processes including regulation of neurotrophic factors, neuroprotection, brain development and neuroplasticity indicated to this matter that it might have a role in psychiatric diseases such as schizophrenia and depression and also tiredness, general ache, pains and somatoform disorders. Depression is also associated with hypovitaminosis D, various illnesses such as multiple sclerosis, rheumatoid arthritis heart disease, osteoporosis, diabetes mellitus, and hypertension (8-16).

### Conclusion

Vitamin D is crucial not only for bone health but for proper brain development and psychological functioning. However, low levels of vitamin D are associated with seasonal affective disorder, depression, and schizophrenia in adults, but there is conflicting evidence about the relationship between vitamin D deficiency and psychological disorders. Our review is consistent with the hypothesis that, low vitamin D concentration is associated with psychological disorders, so, scientific databases were searched from 2000 through 2014. Although we did not

address the issue as to whether the observed differences represent a causal relationship between vitamin D deficiency and psychiatric symptoms, the results are however, important given the significance of vitamin D to overall health. We suggest that increased attention should be given to vitamin D deficiency in psychiatric disorders.

### Authors' contributions

NSA; idea and search for previous related articles. MRT; idea and preparing of paper and comments. MZ; writing and editing of paper and references.

### Ethical considerations

Ethical issues (including plagiarism, informed consent, misconduct, double publication and redundancy) have been completely observed by authors.

### Conflict of interests

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### References

1. Holick MF, Chen TC. Vitamin D deficiency: a worldwide problem with health consequences. *Am J Clin Nutr* 2008; 87: 1080S-6S.
2. El-Hajj Fuleihan G. Vitamin D deficiency in the Middle East and Its Health Consequences. In: Holick MF, editor. *Vitamin D: Physiology, Molecular Biology, and Clinical Applications*. New York: Humana Press; 2010; pp. 469-94.
3. Siddiqui AM, Kamfar HZ. Prevalence of vitamin D deficiency rickets in adolescent school girls in Western region, Saudi Arabia. *Saudi Med J* 2007; 28(3): 441-4.
4. Hashemipour S, Larijani B, Adibi H, Sedaghat M, Pajouhi M, Bastan-Hagh MH, *et al*. The status of biochemical parameters in varying degrees of vitamin D deficiency. *J Bone Miner Metab* 2006; 24(3): 213-8.
5. Hosseinpanah F, Rambod M, Hossein-nejad A, Larijani B, Azizi F. Association between vitamin D and bone mineral density in Iranian postmenopausal women. *J Bone Miner Metab* 2008; 26(1): 86-92.
6. Heshmat R, Mohammad K, Majdzadeh SR, Forouzanfar MH, Bahrami A, Ranjbar Omrani GH, *et al*. Vitamin D Deficiency in Iran: A Multi-center Study among Different Urban Areas. *Iran J Public Health* 2008; 37: 72-8.
7. Holick MF. Vitamin D deficiency. *N Engl J Med* 2007; 357(3): 266-81.
8. Eyles DW, Smith S, Kinobe R, Hewison M, McGrath JJ. Distribution of the vitamin D receptor and 1 alpha-hydroxylase in human brain. *J Chem Neuroanat* 2005; 29: 21-30.
9. Ardalan MR, Sanadgol H, Nasri H, Baradaran A, Tamadon MR, Rafeiean-Kopaei R. Vitamin D therapy

- in diabetic kidney disease; current knowledge on a public health problem. *J Parathyroid Dis* 2014; 2(1): 15-17.
10. Fernandes de Abreu DA, Eyles D, Feron F. Vitamin D, a neuroimmunomodulator: implications for neurodegenerative and autoimmune diseases. *Psychoneuroendocrinology* 2009; 34 (suppl 1): S265-77.
  11. Wilkins CH, Sheline YI, Roe CM, Birge SJ, Morris JC. Vitamin D deficiency is associated with low mood and worse cognitive performance in older adults. *Am J Geriatr Psychiatry* 2006; 14: 1032-40.
  12. Milaneschi Y, Shardell M, Corsi AM, Vazzana R, Bandinelli S, Guralnik JM, *et al.* Serum 25-Hydroxyvitamin D and depressive symptoms in older women and men. *J Clin Endocrinol Metab* 2010; 95: 3225-33.
  13. Nanri A, Mizoue T, Matsushita Y, Poudel-Tandukar K, Sato M, Ohta M, *et al.* Association between serum 25-hydroxyvitamin D and depressive symptoms by survey season. *Eur J Clin Nutr* 2009; 63: 1444-7.
  14. Chan R, Chan D, Woo J, Ohlsson C, Mellstrom D, Kwok T, *et al.* Association between serum 25-hydroxyvitamin D and psychological health in older Chinese men in a cohort study. *J Affect Disord* 2011; 130: 251-9.
  15. Barnard K, Colon-Emeric C. Extraskelatal effects of vitamin D in older adults: cardiovascular disease, mortality, mood, and cognition. *Am J Geriatr Pharmacother* 2010; 8: 4-33.
  16. Howland RH. Vitamin D and depression. *J Psychosoc Nurs Ment Health Serv* 2011; 49: 15-8.
  17. McCann J, Ames B. Is there convincing biological or behavioral evidence linking vitamin D deficiency to brain dysfunction? *FASEB J* 2008, 22: 982-1001.
  18. Pan A, Lu L, Franco OH, Yu Z, Li H, Lin X. Association between depressive symptoms and 25-hydroxyvitamin D in middle-aged and elderly Chinese. *J Affect Disord* 2009; 118: 240-3.
  19. Yamshchikov AV, Desai NS, Blumberg HM, Ziegler TR, Tangpricha V. Vitamin D for treatment and prevention of infectious diseases: a systematic review of randomized controlled trials. *Endocr Pract* 2009; 15: 438-49.
  20. Stewart R, Hirani V. Relationship between vitamin D levels and depressive symptoms in older residents from a national survey population. *Psychosom Med* 2010; 72(7): 608-12.
  21. Lee DM, Tajar A, O'Neill TW, O'Connor DB, Bartfai G, Boonen S, *et al.* lower vitamin D levels are associated with depression among community-dwelling European men. *J Psychopharmacol* 2011, 25(10): 1320-8.
  22. Kjaergaard M, Joakimsen R, Jorde R. Low serum 25-hydroxyvitamin D levels are associated with depression in an adult Norwegian population. *Psychiatry Res* 2011; 190(2-3): 221-5.
  23. Anglin RE, Samaan Z, Walter SD, McDonald SD. Vitamin D deficiency and depression in adults: systematic review and meta-analysis. *Br J Psychiatry* 2013; 202: 100-7.
  24. Buell JS, Scott TM, Dawson-Hughes B, Dallal GE, Rosenberg IH, Folstein MF, *et al.* Vitamin D is associated with cognitive function in elders receiving home health services. *J Gerontol A Biol Sci Med Sci* 2009; 64(8): 888-95.
  25. Annweiler C, Schott AM, Allali G, Bridenbaugh SA, Kressig RW, Allain P, *et al.* Association of vitamin D deficiency with cognitive impairment in older women: cross-sectional study. *Neurology* 2010; 74(1): 27-32.
  26. Llewellyn DJ, Lang IA, Langa KM, Melzer D. Vitamin D and cognitive impairment in the elderly U.S. population. *J Gerontol A Biol Sci Med Sci* 2011; 66(1): 59-65.
  27. Eskandari F, Martinez PE, Torvik S, Phillips TM, Sternberg EM, Mistry S, *et al.* Low bone mass in premenopausal women with depression. *Arch Intern Med* 2007; 167: 2329-36.
  28. Mozaffari-Khosravi H, Nabizade L, Yassini-Ardakani SM, Hadinedoushan H, Barzegar K. The effect of 2 different single injections of high dose of vitamin D on improving the depression in depressed patients with vitamin D deficiency: a randomized clinical trial. *J Clin Psychopharmacol* 2013; 33(3): 378-85.
  29. Kalueff AV, Keisala T, Minasyan A, Kuuslahti M, Miettinen S, Tuohimaa P. Behavioural anomalies in mice evoked by "Tokyo" disruption of the Vitamin D receptor gene. *Neurosci Res* 2006; 54(4): 254-60.
  30. Keisala T, Minasyan A, Järvelin U, Wang J, Hämäläinen T, Kalueff AV, *et al.* Aberrant nest building and prolactin secretion in vitamin D receptor mutant mice. *J Steroid Biochem Mol Biol* 2007; 104(3-5):269-73.
  31. Kalueff A, Loseva E, Haapasalo H, Rantala I, Keranen J, Lou YR, *et al.* Thalamic calcification in vitamin D receptor knockout mice. *Neuroreport* 2006; 17(7): 717-21.
  32. Berg AO, Melle I, Torjesen PA, Lien L, Hauff E, Andreassen OA. A cross sectional study of vitamin D deficiency among immigrants and Norwegians with psychosis compared to the general population. *J Clin Psychiatry* 2010; 71(12): 1598-604.
  33. Hedelin M, Lof M, Olsson M, Lewander T, Nilsson B, Hultman CM, *et al.* Dietary intake of fish, omega-3, omega-6 polyunsaturated fatty acids and vitamin D and the prevalence of psychotic-like symptoms in a cohort of 33,000 women from the general population. *BMC Psychiatry* 2010; 10: 38.
  34. Itzhaky D, Amital D, Gorden K, Bogomolni A, Arnson Y, Amital H. Low serum vitamin D concentrations in patients with schizophrenia. *Isr Med Assoc J* 2012; 14(2): 88-92.
  35. McGrath J, Saari K, Hakko H, Jokelainen J, Jones

- P, Järvelin MR, *et al.* Vitamin D supplementation during the first year of life and risk of schizophrenia: a Finnish birth cohort study. *Schizophr Res* 2004; 67(2-3): 237-45.
36. Yüksel RN, Altunsoy N, Tikir B, Cingi Külük M, Unal K, Goka S, *et al.* Correlation between total vitamin D levels and psychotic psychopathology in patients with schizophrenia: therapeutic implications for add-on vitamin D augmentation. *Ther Adv Psychopharmacol* 2014; 4(6): 268-75.
37. Norelli LJ, Coates AD, Kovasznay BM. A comparison of 25-hydroxyvitamin D serum levels in acute and long-stay psychiatric inpatients: a preliminary investigation. *e-SPEN* 2010; 5(4): e187-9.
38. Kendell RE, Adams W. Exposure to sunlight, vitamin D and schizophrenia. *Schizophr Res* 2002; 54(3): 193-8.
39. Gracious BL, Finucane TL, Friedman-Campbell M, Messing S, Parkhurst MN. Vitamin D deficiency and psychotic features in mentally ill adolescents: a cross-sectional study. *BMC Psychiatry* 2012; 12: 38.
40. Jorde R, Sneve M, Figenschau Y, Svartberg J, Waterloo K. Effects of vitamin D supplementation on symptoms of depression in overweight and obese subjects: randomized double blind trial. *J Intern Med* 2008; 264(6): 599-609.