

# Vitamin-D Deficiency and Its Association with Depression in Under 18s: A Mysterious Relationship of Sunlight with Darkness

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## Abstract

Vitamin D receptors are present in areas of the brain involved in mood regulation, such as the hippocampus and prefrontal cortex. It is suggested that Vitamin D may modulate the synthesis and release of neurotransmitters, including serotonin, dopamine, and norepinephrine, which play crucial roles in mood regulation and are implicated in depression. Vitamin D also has anti-inflammatory properties and can influence immune system functioning. Chronic inflammation has been linked to the development of depression. Vitamin D may help regulate the immune response, reducing inflammation and potentially mitigating depressive symptoms. The deficiency of this vitamin has been previously thought to be not as common as recognized now. This review looked at several studies to explore the association of Vitamin D deficiency and clinical depression in children and adolescents. Many studies based on adult population have found plausible link between Vitamin D deficiency and depression but the research in under 18s have been limited. Based on the available research, mental health clinicians need to maintain a high clinical suspicion, to make early diagnosis and treatment of vitamin D deficiency.

**Keywords:** depression; under 18s; vitamin D deficiency; child and adolescent

## Introduction

Vitamin D (also known as sunshine vitamin) is a group of fat-soluble secosteroids responsible for increasing intestinal absorption of calcium, magnesium, and phosphate, and many other biological effects [1,2,3]. In humans, the most important compounds in this group are vitamin D<sub>3</sub> (cholecalciferol) and vitamin D<sub>2</sub> (ergocalciferol) [2,3,4]. The major natural source of the vitamin is synthesis of cholecalciferol in the lower layers of epidermis of the skin, through a photo-chemical reaction of UVB light, from the sun exposure (specifically UVB radiation) or UVB lamps. [1] Cholecalciferol and ergocalciferol can be ingested from the diet and supplements. The UK government states: "everyone is advised to take a supplement of vitamin D during winter months" [5].

### Prevalence of Vit D deficiency

Results from a 4-year rolling program (2008/2009 – 2011/2012) showed 7.5% of children aged 1.5–3 years, 14% of children aged 4–10 years, and 22% of children aged 11–18 years had a serum 25(OH)D concentration below 25 nmol/L. When subdivided by season, in the winter months of January to March, this increased to 40% of children aged 11–18 years, compared with 13.4% in the summer months, of July to September, for the same age group [6]. A primary

care database cohort study (n = 711,788) of children 0–17 years in England found the incidence rate of vitamin D deficiency increased from 3.14 per 100,000 person-years in 2000 to 261 per 100,000 person-years in 2014 [7].

Depression is one of the most prevalent mental health disorders that affects individuals of all age groups, including children and adolescents. Approximately 280 million people in the world have depression [8]. An estimated 3.8% of the population experience depression, including 5% of adults (4% among men and 6% among women), and 5.7% of adults older than 60 years. The prevalence of depressive disorder (DD) is 5.7% among those aged 13–18 years old [9, 10]. In autumn 2022, around 1 in 6 (16%) adults aged 16 years and over reported moderate to severe depressive symptoms (Office of National statistics UK-[11]. The prevalence of childhood depression has been estimated to be 1% in pre-pubertal children and around 3% in post-pubertal young people (NICE-2020) [12]. Approximately 7.6% of children aged 12 years and older have had moderate to severe depression [13].

### Depression and Vitamin D

Depression during childhood and adolescence can have far-reaching consequences, negatively affecting academic performance, social interactions, and

overall quality of life. Identifying modifiable risk factors and potential interventions is crucial for the early detection and management of depressive symptoms in this age group. Recent studies have shown that people residing at higher latitudes are more vulnerable to depression attributed to seasonal change, especially during the winter solstice [17,18]. One such factor that has attracted considerable attention in recent years is the role of vitamin D. As an essential nutrient, vitamin D plays a critical role in maintaining optimal bone health and supporting the proper functioning of the immune system. However, emerging evidence suggests that vitamin D may also be involved in the pathophysiology of mental health disorders, particularly depression.

### Why this review?

The three pertinent questions I have tried to find answers to through this review include:

“Has vitamin D deficiency got any association with depression in under 18s?”

“What’s the nature of this association i.e., is it etiological or consequential?”

“Can vitamin D supplementation reduce the risk of depression or improve depressive symptoms in individuals with low vitamin D levels?”

The inclusion criteria included ‘studies that examine the relationship between vitamin D and depression in children and adolescents under 18 years old, studies that report on the prevalence of vitamin D deficiency or insufficiency in children and adolescents with depression, studies that investigate the impact of vitamin D supplementation on depressive symptoms in children and adolescents with low vitamin D levels, studies that were published in peer-reviewed journals, studies that were conducted in humans, studies that were published in English as well as other languages, studies that were published within a certain time frame, such as the past 10 years, observational studies, RCTs, systemic reviews and meta-analysis’.

The exclusion criteria included ‘studies that focus on adults or mixed age groups without separate analysis of children and adolescents, studies that do not report on vitamin D levels or vitamin D supplementation,

studies that do not use validated measures of depression, case reports, editorials, or reviews without original data, studies that include participants with other psychiatric or medical conditions that may confound the relationship between vitamin D and depression, studies that are not original research, such as letters, comments, or opinions, studies that are not focused on depression, but rather on other mental health conditions or outcomes, studies that do not provide information on the sample size, methodology, or statistical analyses performed, studies that were conducted on animal models or in vitro systems, presence of any chronic medical or psychiatric condition other than depression, history of substance misuse, pregnancy or lactation, any medical condition that effects vitamin D metabolism or absorption such as liver or kidney disease’.

### Literature search

Search terms were adapted to suit the search needs of other databases as appropriate. Additionally, hand searches of the reference lists of the generated articles were done in order to ensure a comprehensive search. We used extensive electronic database for the search of papers through MEDLINE, EMBASE, PUBMED, Google Scholar, AMED (OVID), Bielefeld Academic Search Engine (BASE), bioRxiv, CENTRAL, British Library Ethos, CENTRAL (Cochrane Library), ClinicalTrials.gov, DART Europe E-theses portal, Google, International Clinical Trials Research Platform (ICTRP), Open access theses and dissertations, OPENAIRE, Preprints.org, Proquest Index to Theses in UK & Ireland and TRIP database and BNI (British Nursing Index) Proquest. We also searched database for the Grey Literature including Preprints, bioRxiv, DART Europe E theses portal, ICTRP, Open Access Theses & Dissertations, ClinicalTrials.gov and British Library Ethos.

We managed to find a total of 50 papers, however only 8 met our criteria as set out above. Out of the 8 eligible papers, 5 were Observational and 3 were interventional studies.

	Title	Reference	Country	Age	Method
1	Is Sunshine Vitamin Related to Adolescent Depression? A Cross-Sectional Study of Vitamin D Status and Depression Among Rural Adolescents	Tarikere Satyanarayana et al. [21] © Copyright 2023	India	11-18 years	Cross-sectional study
2	A study on 25-OH cholecalciferol levels in children and adolescents with major depressive disorder	Saber Abdel Azim Mohameda et al [22] © 2014 Egyptian Journal of Psychiatry 1110-1105	Egypt	6-18 years	Case-control study
3	Urinary iodine and serum 25-hydroxyvitamin D are associated with depression in adolescents	Wei Huang et al [23] © 2018 Department of Pediatric Care, Zaozhuang City Hospital, Zaozhuang 277100.	China	8 to 16 years	Case-control study
4	The association of serum 25-hydroxyvitamin D3 and D2 with depressive symptoms in childhood a prospective cohort study	Anna-Maija Tolppanen et al [20] © 2011 The Authors. Journal of Child Psychology and Psychiatry	UK	7- 16 years	prospective cohort study
5	Vitamin D level in relation to depression symptoms during adolescence	Reem Al-Sabah1 et al [19] © 2022 Faculty of Medicine, Kuwait University, Kuwait, Kuwait.	Kuwait	11- 16 years	Cross-Sectional study
6	Effect of vitamin D deficiency on depressive symptoms in child and adolescent psychiatric patients: results of a randomized controlled trial	Lars Libuda et al [24] Department of Child and Adolescent Psychiatry, University Hospital Essen, Germany © 2020	Germany	11- 18.9 years	Randomized controlled study
7	High Dose Vitamin D Supplementation Is Associated with a Reduction in Depression Score Among Adolescent Girls: A Nine-Week Follow-Up Study	Afsane Bahrami et al [25] Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, © 2018	Iran	12-16 years	Before-after (pre-post) study
8	Depressed adolescents in a case-series were low in vitamin D and depression was ameliorated by vitamin D supplementation	Göran Högberg et al [26] Acta Paediatrica © 2012	Sweden	10-19 years	Before-after (pre-post) study

## Review and discussion

Within the scope of our investigation, a total of 58 articles were subjected to rigorous scrutiny to ascertain their relevance in elucidating the association between vitamin D deficiency and depression in under children and adolescents. Only 8 articles fulfilled the predefined criteria set out above, thereby highlighting paucity in research probing this association. It is worth noting that within this selection process, a considerable portion of articles, precisely 28, were deemed unsuitable due to their incorporation of adult subjects, while an additional 22 were excluded as they primarily focused on investigating alternative mental and physical health conditions. The assortment of qualifying articles featured a diversity of research paradigms. Among these, 5 articles adopted an observational study model, employing a multifaceted approach to investigate the potential correlation between vitamin D deficiency and depression. Complementing these

were 3 interventional studies, focusing on investigating the impact of vitamin D supplementation on depression outcomes. Strikingly, the geographic distribution of these studies delineated a global spectrum, with only one but significantly important article hailing from the United Kingdom which was an observational prospective cohort study. The remaining 7 studies hailed from different countries across the globe including Kuwait, Egypt, Iran, Germany, Sweden, China, and India. Upon detailed review of the observational studies, a noteworthy trend emerged. Out of the 5 studies, 4 evinced statistically significant correlations between vitamin D deficiency and depression, underscoring a promising avenue for further exploration. However, one study Reem Al-Sabah1 et al [19] failed to substantiate any discernible association. Central to our primary inquiry was the fundamental elucidation of the association between vitamin D deficiency and depression. While 80% of the included observational

studies provided statistical evidence supporting a plausible correlation, inherent limitations concerning study design, sample size, and heterogeneity warrant cautious interpretation. Notably, none of the studies definitively established the nature of this relationship. Notwithstanding, one study (20) notably employed a prospective cohort design while the remainder predominantly relied on cross-sectional methodologies, constraining the depth of insights into causality.

Highlighting a pivotal contribution within the observational studies is the prospective cohort study conducted by Anna-Maija Tolppanen et al [20] in England, highlighting the significance of investigating the association of Vitamin D deficiency and depression during childhood and adolescence. This article emphasised on the fact that association of depression and Vitamin D deficiency can be better studied in children and adolescents because confounders such as alcohol, smoking and mood-altering drugs are somewhat less likely than in adult populations. Furthermore, the imperative of recognizing the emergence of depression during these formative years was underscored, thereby emphasizing the potential efficacy of early preventive interventions initiated during this critical developmental phase. In this prospective study of children, they found higher concentrations of season-adjusted 25(OH)D<sub>3</sub>, assessed at a mean age of 9.8 years, to be associated with lower levels of depressive symptoms at age 13.8 years and with increased odds of decreasing symptoms between age 10.6 and 13.8 years. These associations were independent of a wide range of potential confounders, as well as of 25(OH)D<sub>2</sub>, calcium, phosphate and PTH concentrations, which were not strongly associated with depressive symptoms at either age. They also found that less meticulous protection from UVB was associated with lower PTH concentrations and higher 25(OH)D<sub>3</sub> concentrations. One of the interesting but understandable result was that children who spent more time outdoors during summer had higher 25(OH)D<sub>3</sub> and 25(OH)D<sub>2</sub> concentrations and those who spent more time outdoors during summer had lower risk of depressive symptoms at age 13.8 years. Consistent with these findings and reflecting on the fact that 25(OH)D<sub>3</sub> is the biggest contributor to total 25(OH)D, they found that risk of depressive symptoms was greater at 13.8 years in those with total 25(OH)D deficiency or total 25(OH) D insufficiency. Depressive symptoms at age 10.6 years, did not differ

between those with total vitamin D deficiency or insufficiency, whereas those with deficiency or insufficiency had increased risk of depressive symptoms of 20-30% at age 13.8. The association of 25(OH)D<sub>3</sub> with depressive symptoms in children only emerged with symptoms measured 3 years after exposure assessment and was not present when symptoms were assessed just 1 year after exposure assessment. One might expect a stronger association with the earlier age, possibly in part because of reverse causality [i.e., depressive symptoms resulting in less outdoor activity and hence reduced vitamin 25(OH)D<sub>3</sub> concentrations]

One of the strengths of this study included that it was the first prospective cohort study with a large sample size (the cohort consisted of 14,062 live births from 14,541 enrolled pregnant women who were expected to give birth between 1 April 1991 and 31 December 1992) and complete data on outcomes, exposures and confounders were available from 2,759 and 2,752 children, respectively, for assessment with outcomes at 10.6 years and with outcomes at 13.8 years. The other strengths in this study include examination of potential confounding by a wide range of characteristics, self-reported, rather than parent-reported depressive symptoms and the finding of 27% of the sample having vitamin D deficiency (concentration below 20 ng/ml) which suggests that results can be applied to a population where vitamin D deficiency is common. This study however did highlight the limitations including analysing depressive symptoms as a categorical variable instead of a continuous score, which might have lost some refinement, but this was necessary due to highly skewed distribution. The other weakness in the study was measurement of serum 25(OH)D<sub>3</sub>, D<sub>2</sub>, phosphate, calcium and PTH on a single occasion which may not accurately reflect usual status. The results do not imply causality and the association of 25(OH)D<sub>3</sub> with depressive symptoms 3 years later might be explained by residual confounding. They did not use diagnostic interview rather self-reported questionnaire.

The remaining 4 out of 5 articles have been cross sectional models with relatively small sample sizes but some of these did show statistically significant results. *Tarikere Satyanarayana et al [21]* an article from India studied 451 adolescents who were aged 11-18 years. One of the odd features of this article is the definition of vitamin D insufficiency and deficiency. They defined less than 20 ng/ml as 'insufficiency' while

according to The International Association of Endocrinology this is defined as 'deficiency'. They found that out of 451 adolescents, 14.6% had vitamin D deficiency and 35.9% had insufficiency. Out of 133 having severe depression (score of 31-40 on BDI-II) 11% were found to have vitamin D deficiency and 48.1% had vitamin D insufficiency. The other interesting point and that is the multinomial logistic regression analysis of various factors with depression indicated that the odds of severe depressions was 2.82 (p value 0.001) in those with vitamin D deficiency and the odds of severe depression was 3.42 (p value 0.001) in females with vitamin D deficiency. The study did not show temporal relationship however it did show a statistically significant but inconsistent relationship between vitamin D deficiency and Depression.

This study showed that vitamin D deficiency had a statistically significant association with depression, with students who were studying in the 9th standard and exercising in the afternoon having higher odds of minimal depression, those who were exercising in the afternoon having higher odds of moderate depression and those who were females and had vitamin D deficiency (VDD) had higher odds of having severe depression. They also found a paradoxical result that among adolescent school children, those who were exercising in the afternoon had higher odds of having moderate depression. The association between vitamin D deficiency and Depression according to this study is irregular and does not signify its association with covariables. The other weakness in this study includes a relatively smaller sample size taken from the same geographic terrain hinders the generalisation of study results. The results from this study to establish association between vitamin D deficiency and depression are equivocal due to the study design, and failure to study other covariables such physical health, social factors like relation with father, mother, and school performance etc. which could have played a role in depression, which were not assessed in the present study.

Saber Abdel Azim Mohameda et al [22] studied vitamin D levels in 82 children and adolescents with major depressive disorder and in 21 age-matched and sex-matched healthy controls and found that vitamin D levels and the severity of depression were inversely correlated; the more severe the depression was, the lower was the level of vitamin D (Statistically significant as P-value was 0.0001). This study concluded that there was high statistically significant (p value 0.0001) difference in the severity of

depression, and both HDRS and vitamin D levels – the higher the level of HDRS, the more severe the degree of depression and conversely the lower the level of vitamin D, the more severe the degree of depression. The strengths of this study included case and control methodology as well as use of semi structured clinical interview (based on DSM-IV-TR) with clinicians and HDRS (reliable scale of severity of depression). Though this study did establish the association between vitamin D deficiency and depression but failed to show the nature of the association. The weakness in this study despite consistent results with other results from adult studies, include its small sample, cross sectional design, using outpatient sampling, absence of information on seasonal vitamin D levels, sun exposure, skin colour and lack of parathyroid hormone and calcium level measurement.

Wei Huang et al [23] studied whether depressive disorder (DD) in adolescents is associated with the levels of serum 25-hydroxyvitamin D [25(OH)D] and urinary iodine. In the case control cross sectional study, they studied 160 adolescents (75 males and 85 females) diagnosed with depressive disorder (DD) 110 healthy control subjects (50 males and 60 females). Adolescents who received medical treatments that could affect thyroid function in the preceding 2 months were excluded. Adolescents with suicidal ideation were also excluded. The results indicated that females with DD had a higher BMI (p = 0.04) and that tobacco use was more frequent in females with DD than control subjects (p = 0.01). The important finding of this study was the difference between the mean concentrations of total serum 25(OH)D [25(OH)D<sub>2</sub> + 25(OH)D<sub>3</sub>] in DD and control participants which were 17.4 ± 4.3 and 22.9 ± 5.0 ng/mL respectively. In addition, the mean concentrations of urinary iodine in DD and control participants were 175.7 ± 66.5 and 250.8 ± 88.6 ng/mL, respectively. The results indicate that both serum 25(OH)D and urinary iodine levels were significantly lower in D adolescents than in the control subjects, suggesting a close relationship between DD 25(OH)D, and iodine levels in vivo. DD patients had lower concentrations of 25(OH)D<sub>3</sub> (p < 0.005) and urinary iodine (p < 0.05) than non-DD control, in both male and female cohorts. However, serum 25(OH)D<sub>2</sub> concentration did not significantly correlate with depressive symptoms which is consistent with what Anna-Maija Tolppanen et al [20] had found. In terms of weaknesses, this study failed

to clarify the mechanism underlying the impact of serum 25(OH)D and urinary iodine levels on DD and establish the nature of the association. Secondly, the depressive symptoms were diagnosed by self-reported questionnaires to screen for depression, which still remains uncertain, and relatively small sample size but despite these limitations, the present study is important in demonstrating that serum 25(OH)D and urinary iodine are both related to depressive symptoms in adolescents at 8 – 16 years of age.

Reem Al-Sabah<sup>1</sup> et al [19] investigated the association between 25-hydroxyvitamin D (25(OH)D) and depression symptoms among adolescents in Kuwait through school based cross-sectional study model by randomly selecting 704 adolescents in middle schools. They found prevalence of depression symptoms in schoolchildren to be 13.35% but according to their results, vitamin D status did not seem to be associated with depression symptoms among adolescents. Association between plasma 25-hydroxyvitamin D and depression symptoms (CDI  $\geq$  19 score) before and after adjusting for potential confounders shows statistically insignificant results as P values are significantly high with wide CI. The other interesting and puzzling results included the association between depression symptoms (CDI  $\geq$  19 score) and socio-demographic factors in adolescents showed statistically insignificant association between the covariables as the P value was much higher. However, the odds ratio is high for females, and lower father income but the P Values make these insignificant. Only maternal education showed inverse statistically significant association with depression symptoms ( $p = 0.021$ ). None of the lifestyle factors including the time spent on physical activity ( $p = 0.461$ ), time spent on sedentary activities ( $p = 0.714$ ) or body mass index (BMI) categories ( $p = 0.185$ ) was significantly associated with depression symptoms in invariable analysis, which have been different from the results of other studies in this review as well as several other studies in the adult population. Other inconsistent findings from this study except for PTH, calcium, vitamin B12, anaemia, iron, ferritin and folate were all not significantly associated with depression symptoms. (Odds ratio for PTH was 1.04 with P-value of 0.023, while for the others P - value ranged between 0.12 to 0.79, statistically insignificant. Association between depression symptoms (CDI  $\geq$  19 score) and lifestyle factors, physical activity, body mass Index (food intake, walking to school, watching tv etc) all with P values well above 0.05, and with paradoxical

odds ratios making these statistically and clinically insignificant.

Strengths of this study included using a relatively large sample (704 schoolchildren) and using quantile regression to model the CDI score as a continuous, rather than a binary outcome. Weaknesses of this study included cross sectional model, and lack of information about the history of depression in the parents or the siblings, exposure to early childhood adversity experience (such as abuse, neglect, the loss of a loved one in early life), which are potential risk factors for depression and use of the CDI without a diagnostic interview. It is possible that many of the children with severe depression symptoms were absent from school during the study period, which may have attenuated the association.

Out of the three interventional studies, only one was RCT while the two were non- RCT. Lars Libuda et al [24] examined the effect of an untreated vitamin D deficiency compared to an immediate vitamin D3 supplementation on depression scores in children and adolescents during standard day and in-patient psychiatric treatment through double blind RCT- reportedly the first RCT to study this effect in children and adolescents. Patients with vitamin D deficiency [25(OH)D  $\leq$  30 nmol/l] and at least mild depression [BDI-II  $>$  13] ( $n = 113$ ) were 1:1 randomised into verum (VG; 2640 IU vitamin D3/d) or placebo group (PG) in a double-blind manner. The main finding of this study was that an immediate vitamin D3 supplementation in depressed child and adolescent psychiatric patients with vitamin D deficiency did not result in a significant decrease of self-reported depressive symptoms, but in a statistically significant decrease of parent-reported depressive symptoms after 4 weeks of in- or day-patient treatment compared to placebo (P - value of 0.016). In conclusion, results on potential antidepressant effect of vitamin D supplementation remain conflicting. While self-rated depression improved similarly in both the verum and the placebo groups of this study, the observed differences in parent-reported depressive symptoms in favour of vitamin D supplementation warrant attention. The heterogeneity of depression and depressive symptoms as well as of their specific underlying pathophysiologic mechanism could represent another explanation for the lack of a positive finding in this study. The strength of this study includes the double blind RCT model. 113 was the sample size which for an RCT not too bad.

Afsane Bahrami et al [25] studied to evaluate the effectiveness of high dose vitamin D supplementation on depression and aggression scores in adolescent girls. Participants were selected using a cluster randomised sampling method from various regions within the cities of Mashhad and Sabzevar, Iran. Among the cohort of 1,026 girls initially considered for inclusion, 988 fulfilled the inclusion criteria and participated in the intervention phase; 940 participants completed the intervention which was vitamin D supplementation- 50000 iU/week for 9 weeks. They found a significant reduction of BDI scores in severe depression, and moderate depression with P value of 0.001 i.e., severe depression score of 33 was reduced to 26 and moderate depression score of 23 was reduced to 20 after the intervention (with P- value of 0.001). They also found a positive significant association between total depression score and total aggression score ( $r = .39, p > .001$ ) at baseline study. The article mentions about some biological evidence for a causal contribution of vitamin D deficiency in depression but did not provide any reference. There was a significant increase in the median serum 25 (OH) vitamin D concentrations (6.7 ng/mL at baseline vs. 35.5 ng/mL after intervention;  $p > .001$ ) which indicated good adherence to vitamin D supplementation. There were no details of the actual baseline vitamin D levels or exact number of subjects having vitamin D deficiency or insufficiency. Also, one of the important questions is that how valid and ethically appropriate is to treat people with moderate and severe depression with vitamin D only? They also did not give any reason to why they selected only girls. The other main limitation or weakness of the present study was the absence of a placebo group for comparing with the intervention group. We could not have a placebo group because of ethical considerations. How ethical is to treat those with moderate to severe depression with vitamin D only? Strengths of this study includes large sample size, a population-based study, subgroup analysis, and focus on a specific population (girls only - homogeneous group).

Göran Högberg et al [26] studied the relationship between depression in adolescents and vitamin D in a case-series that included effects of vitamin D supplementation. Fifty-four cases of depressed Swedish adolescents (37 girls and 17 boys) were examined for psychiatric and somatic evaluation. Among them, 19 were considered by the clinicians to suffer from moderate depression and 35 from severe

depression. Criteria for severe depression were suicidal ideation and suicide attempts. On investigation for Vitamin D levels, 48 were found to have Vit D deficiency (25OHD levels below 60nmol/L) and were offered vitamin D3 over 3 months. They continued with their standard treatment that included psychotherapy or supportive counselling and, in some cases, also medication (methylphenidate for comorbid attention-deficit disorder in two cases, the antidepressant fluoxetine in three cases and duloxetine in one case).

Depressive symptoms and wellbeing were assessed by using MFQ-S and WHO-5. MFQ-S scores (the lower the better) showed an average mean of 14.7 before vitamin D3 supplementation and 7.1 after the supplementation, statistically significant with a p-value of 0.05. WHO-5 scores (the higher the better) with a mean value of 25 before supplementation and 43 after supplementation which were statistically highly significant with a p-value of  $<0.001$ . Another finding of interest is the significant decrease in the item 'difficulties to concentrate' as it might indicate a role of vitamin D in adolescent attention-deficit disorders. An interesting finding in this series is the nonsignificant effect of season on the levels of 25OHD. They hypothesise that depressed adolescents might have a sun-avoiding lifestyle, spending a greater amount of time indoors and perhaps in nighttime spent in front of the computer. One of the other interesting findings in this study was that 11% of the subjects were suffering from severe vitamin D deficiency ( $<25$  nmol/L). This finding on its own raises the important question whether routine assessment of vitamin D status should be carried out in depressed adolescents.

## Conclusion

In my opinion, this literature review indeed highlighted a notable trend across the majority of the examined articles, wherein 75% (six out of eight studies) exhibited a statistically significant association between vitamin D deficiency and depression among children and adolescents. However, the conclusions drawn from these findings necessitate a cautious approach due to several inherent limitations in the studies. These limitations encompass the predominant use of cross-sectional models, small sample sizes, potential residual confounders, and the absence of more randomized controlled trials (RCTs). Additionally, the limited body of research focusing

specifically on individuals under the age of 18 further compounds the challenge of establishing a concrete causal relationship between vitamin D deficiency and depression in this demographic.

Given the observed trends in these studies, a potential recommendation emerging from this analysis involves considering routine assessment of vitamin D levels in children and adolescents experiencing depression. This recommendation stems from the statistical significance observed in the majority of the reviewed articles despite the limitations highlighted. However, implementing routine vitamin D level checks should be approached with caution and should ideally be part of a broader diagnostic assessment for depression in this age group, considering the multifactorial nature of mental health conditions. Further robust research, preferably incorporating larger sample sizes, longitudinal designs, and RCTs, is crucial to elucidate the nature and causality of the relationship between vitamin D deficiency and depression in children and adolescents, thus facilitating more informed and targeted interventions.

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