

SYSTEMATIC REVIEW

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Risk of suicide, suicide attempt, and suicidal ideation among people with vitamin D deficiency: a systematic review and meta-analysis

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Abstract

Background Evidence shows that vitamin D affects brain function. Transcription of over 1000 genes is known to be controlled by vitamin D, potentially contributing to the neurotrophic and neuroprotective effects that can influence suicidal behavior. Several investigations with contradicting findings have identified an association between suicidal behaviors (SBs) or depressive symptoms and low vitamin D levels. This meta-analysis aimed to analyze the pooled association between vitamin D deficiency and the risk of suicide, suicide attempt (SA), and suicidal ideation (SI).

Methods A systematic search was performed through PubMed, Web of science (ISI), Scopus, Embase, and grey literature up to 10 October 2024. Meta-analysis included observational studies that assessed the association between SBs and vitamin D blood serum level and/or vitamin D deficiency. After screening and quality assessment, meta-analysis and sensitivity analysis using random effects model were carried out to estimate the pooled odds ratios (ORs) for the risk of suicide, SA, and SI. We also calculated pooled standard mean difference (SMD) of vitamin D levels between control subjects and patients with SBs.

Results A total of 14,095 records were identified. Finally, 13 studies participating 515,406 subjects were included in the meta-analysis after eligibility assessment. Vitamin D deficiency non-significantly increased the risk of suicide, SA, and SI (OR = 1.7; 95% CI: 0.93 – 3.12), (OR = 1.65; 95% CI: 0.98 – 2.80), and (OR = 1.15; 95% CI: 0.94 – 1.41), respectively. However, levels of vitamin D in patients with SBs were significantly lower than in controls without any SBs (SMD = -0.69; 95% CI: -0.89 – -0.49).

Conclusion The results of this meta-analysis indicated that vitamin D levels are lower among patients with SBs. These findings can inform suicide prevention programs, particularly for target groups experiencing significant vitamin D deficiency.

Keywords Suicide, Vitamin D, Suicidal behaviors, Mental illness

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Introduction

Suicide is a major public health concern worldwide [1]. At present, suicide is the second leading cause of death among young people aged 15–29 years at global level [2]. The global age-standardized suicide rate for 2019 was 9.0 per 100,000 population, whereas the age-adjusted suicide rate rose to 14.21 per 100,000 people in 2022 [3–6].

Suicide is a complex and multifactorial phenomenon. Current findings indicate a wide range of predisposing and precipitating factors associated with suicide, with notable differences in their strength of associations [7, 8]. For example, a meta-analysis confirmed that clinical factors such as mental illness and a history of self-harm with an odds ratio (OR) of 13.1 and 10.1, respectively, are the strongest predictors of suicide [9]. Besides clinical risk factors, socio-demographic status, family history, and negative and stressful life events are other domains for the risk of suicide [9, 10].

In previous findings, vitamin D deficiency has been proposed as a risk factor or facilitator of the risk of suicide and suicidal behaviors (SBs), as well as for creating suicidal ideation (SI), although results have been conflicting [11–13]. Evidence shows that vitamin D affects brain function. Transcription of over 1000 genes is known to be controlled by vitamin D, potentially contributing to the neurotrophic and neuroprotective effects that can influence SB [14]. Several studies have identified an association between SBs or depressive symptoms and low vitamin D levels [15–18]. Evidence has shown that some people who die by suicide are those whose vitamin D levels are lower [19]. In a study of 157,211 healthy Korean soldiers, those whose serum vitamin D levels were less than 10 ng/ml experienced a significantly increased risk of suicidal ideation [20]. In a case–control study, the case group was people with suicidal attempts (SAs) and the control group was people without SAs; the average level of vitamin D in the suicide group was significantly lower than the control group. There was a statistically significant relationship between vitamin D levels, the presence of psychiatric illness, and previous SAs [21].

There are conflicting findings regarding the relationship between vitamin D deficiency and suicide risk. Besides, the previous original and/or review studies had two significant flaws: first, they failed to present pooled measures of associations in the form of effect sizes such as odds ratio (OR) and risk ratio (RR), and presenting separately for SA and SI. Secondly, the limited number of eligible primary studies in prior research has made it challenging to draw accurate and realistic conclusions. Therefore, this systematic review and meta-analysis aimed to estimate pooled effect sizes of vitamin D deficiency on the risk of suicide, SA, and SI and standard

mean difference (SMD) of vitamin D blood serum levels between suicidal patients and healthy controls.

Methods

Search strategy

The study systematically searched databases including PubMed, Scopus, Web of Science (ISI), Google Scholar, and Embase from the database beginning up to the date of 10 October 2024. Moreover, Grey literature (open Grey website, Google free search, and Congress) and the reference lists of the final identified records were screened to find more relevant records. The review protocol was developed and adhered to during the review process in accordance with the approved protocol guidelines at Tabriz University of Medical Sciences under number 72632.

The study systematically searched for observational studies that reported the association between vitamin D serum levels and various suicidal behaviors (SBs), including suicide, suicide attempts (SA), and suicidal ideation (SI). The preliminary search terms were “suicide” and “vitamin D” in the title and/or abstract. The final search used the relevant MeSH terms and text words related to suicide and vitamin D deficiency and blood serum level using PICO structure. The study population (P) was people with any suicidal behaviors; intervention/exposure (I) was vitamin D deficiency and/or blood serum levels of vitamin D; and the outcome (O) was any SBs including SI, SA, suicide death, and self-harm. Details for search strategy was presented in Appendix 1. There were no language restrictions.

Eligibility

We included any articles that assessed the association between SBs and vitamin D blood serum level and/or vitamin D deficiency. Eligible studies have reported vitamin D blood serum status on a continuous scale and/or categorized it into vitamin D deficiency and sufficient groups. In the majority of the eligible studies, vitamin D deficiency has been defined as < 20 ng/ml. The review excluded in vitro and gene expression studies, as well as reviews, letters, commentaries, editorials, and qualitative studies. We also excluded any records that reported incomplete data and/or there were no outcomes measures such as vitamin D levels and SBs.

Comparison

Vitamin D levels were used as an exposure variable for comparison between case and control groups. The cases were patients with SBs (suicide, SA, and SI) and controls were healthy people and/or patients without any SBs. We also compared continuous levels of vitamin D between patients with SB and control subjects.

Outcomes

The primary outcomes were suicide, SA, and SI using absolute measures of associations such as odds ratio (OR), relative risk and/or risk ratio (RR) with 95% confidence intervals (CIs). The secondary outcome was the standard mean difference (SMD) of vitamin D serum levels between groups.

Data selection and extraction

Identified records were screened in a blinded and standardized way by two reviewers (HA, JY) independently. The title and abstract of the relevant records are used for screening. Data extracted involved the study title, first author name, year, country, study design, study population and groups, age, sample size, vitamin D serum levels by the original studies measured scale, and effect sizes including OR, RR and mean difference (MD).

Quality and risk of bias assessment

The quality of the included articles was assessed using the modified Downs and Black checklist [22] and previous meta-analysis [23]. The checklist was designed to model judgments according to the grading of recommendations, assessment, development, and evaluations (GRADE) criteria and comprises the following domains: a) Reporting b) External validity c) Internal validity (bias) d) Internal validity (confounding- selection bias), and e) Power. Following the original guidance by Downs and Black, (though with a slight variation), we derived an overall summary risk of bias judgment (excellent; good; fair; poor) for each specific outcome, whereby the overall risk of bias for each study was determined by the highest risk of bias level in any of the domains that were assessed. Details of the quality and risk of bias assessment were presented in Table 2. All of the instrument items were evaluated in a blinded, standardized way by two authors (HA and JY) who were Epidemiologists. The final studies included were decided upon by the consensus of the two authors. If there were any disagreements regarding the final inclusion of the records, the third author (SNM) would make the final decision to include the records.

Statistical analysis

Meta-analysis using a random-effects model was used to estimate the pooled odds ratios (ORs) with 95% CIs for the association between vitamin D deficiency and risk of suicide, SA, and SI. Since the eligible studies have used different scales for assessing vitamin D blood serum levels, the Standardized Mean Differences (SMD) was used. SMD represents the change in scores difference between the case and control groups.

SMD has calculated the difference of values between groups divided into pooled Standard Deviation (SD). Cochran's Q test and I^2 were performed for heterogeneity between studies assessing [24]. All analyses were performed using STATA version 14 (Stata Corp, College Station, TX, USA).

Results

Descriptive and systematic search results

A total of 14,095 records were screened for eligibility. Of those, 23 full-text articles were evaluated for eligibility after screening and removing based on title and abstract. Finally, 13 studies [11–13, 20, 21, 25–32] were included in the systematic review and meta-analysis (see Tables 1 and 2). Figure 1 shows the PRISMA flow diagram of details for the records screening and eligibility assessment process.

Table 1 shows the characteristics of the included studies. A total of 515,406 subjects participated in the review. Target and/or the study groups of the eligible studies were various populations including adults, adolescents, the general population, veterans, military cadres, major depressive disorders (MDD), and schizophrenia patients. However, all eligible studies compared vitamin D deficiency and/or serum levels between SBs patients and control subjects. The scope of publishing articles was between 2013 and 2024. The design of the majority (85%) of eligible articles was case-control or cohort studies. Turkey and USA with 4 and 3 studies had frequently published articles on the association between vitamin D deficiency and SBs, respectively. Out of 13 eligible articles, 10 articles [11, 12, 21, 25–29, 32] concluded that low levels of vitamin D increased SBs, while three articles [11, 20, 29] indicated that although vitamin D levels were lower in suicidal patients compared to controls, no significant associations were found. More details on the summary findings of the included studies are provided in Table 1.

Table 2 presents the results of the quality and risk of bias assessment using the Downs and Black checklist [22], detailing the items for each study. Out of 13 eligible studies, 7 were classified as low risk, 5 as moderate risk, and 1 study was identified as having a high risk of bias, since there were some concerns in the reporting, internal (confounding and the time for blood received from the cases and external validity).

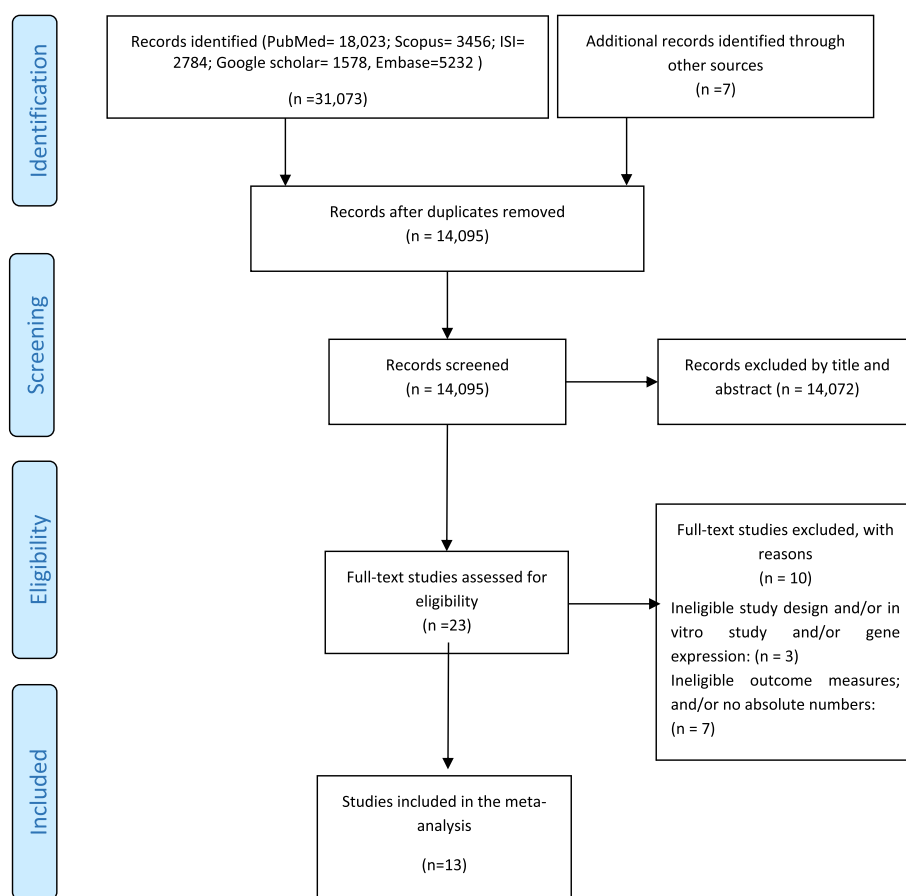
Out of 13 eligible articles, 10 articles reported vitamin D serum levels (continues) and were compared between groups. Regarding suicide, SA, and SI outcomes, 3, 5, and 5 studies reported measures of associations such as OR and/or RR, and absolute numbers between groups, respectively.

Table 1 Characteristics of the included studies

Author	Year	Country	Study design	Study target/ groups	Age (mean)	Sample size	Main findings
Zahoor Ahmed Memon et al. [12]	2024	Pakistan	Cross-sectional	MDD patients with and without suicidal behavior; 55.7% male	44	104	Vitamin-D deficiency is found to be one of the factor for suicidal attempts in patients with Major Depressive Disorder
Lavigne et al. [21]	2023	USA	Retrospective cohort	Veterans (169,241 treated with vitamin D and 169,241 untreated)	61	338,482	Vitamin D supplementation was associated with a reduced risk of suicide attempt and self-harm in veterans
Tansu Gençer et al. [30]	2023	Turkey	Case-control	Suicide attempters (n = 35) and healthy controls (n = 35)	30.5	70	Vitamin D level was found to be significantly lower in suicidal patient
Bagheri et al. [13]	2023	Iran	Case-control	Suicide attempters (n = 171) and healthy people (n = 314)	26.7	471	The study highlighted vitamin D deficiency in the development of suicidal behaviors
Yuan et al. [11]	2023	China	Cohort	Adolescents: 60.8% males	12.5	1426	This study could not confirm the causal effect of vitamin D on suicidality risk among Chinese adolescents
Atik et al. [31]	2020	Turkey	Case-control	59 individuals with suicidal attempt and 42 control; 65% female	30.6	101	Vitamin D deficiency can increase suicidal tendencies in depressed patients
Gokalp [32]	2020	Turkey	Case-control	Adolescents 215 suicide attempters and 200 healthy controls	12.8	415	Vitamin D deficiency may be one of the causes of suicidal behavior in adolescents. Physicians who treat adolescents should consider vitamin D levels in routine examinations
Grudet et al. [29]	2020	USA	Case-control	MDD with (n = 17) and without (n = 31) suicidal ideations; and 54 controls	39.3	102	While vitamin D levels did not significantly differ in MDD vs. controls, lower vitamin D was associated with indices of immune activation in MDD
Kim et al. [20]	2020	Korea	Analytical cross-sectional	Adults With suicidal ideation (n = 6,661); without suicidal ideation (n = 150,550)	39	157,211	Although vitamin D levels were lower in suicidal people, this relationship was not significant
Fond et al. [27]	2019	Turkey	Analytical cross-sectional	Schizophrenia patients	36	251	Vitamin D deficiency is associated with suicide risk
Park et al. [28]	2016	Korea	Case-control	General population (2319 with suicide ideation and 13,374 controls)	49.2	15,693	There were no significant associations between vitamin D, depressive symptoms, and suicidal ideation in Korean adults
Grudet et al. [26]	2014	Sweden	Case-control	Suicide attempters (n = 59), non-suicidal depressed patients (n = 17) and healthy controls (n = 14)	NR	90	Vitamin D deficiency could be a contributing factor to the elevated pro-inflammatory cytokines
John C. Umhau et al. [25]	2013	USA	Nested, case-control	Military personnel (495 suicidal cases and 495 controls)	28.5	990	The lowest levels of vitamin D are associated with an increased risk for suicide

Table 2 Quality and risk of bias assessment of the included studies THE column heading of the last column below is not appropriate and confusing. Insert 'Risk of Bias'

First Author	Year	Reporting	External validity	Internal validity (bias)	Internal validity (confounding)	Risk of bias
Zahoor Ahmed Memon et al. [12]	2024	L	L	L	L	Low
Lavigne et al. [21]	2023	L	M	L	L	Low
Tansu Gençer et al. [30]	2023	L	L	L	M	Low
Bagheri et al. [13]	2023	M	L	L	M	Moderate
Yuan et al. [11]	2023	L	L	H	L	Low
Atik et al. [31]	2020	M	M	L	L	Moderate
Gokalp [32]	2020	L	L	M	L	Low
Grudet et al. [29]	2020	M	L	L	L	Low
Kim et al. [20]	2020	L	L	L	L	Low
Fond et al. [27]	2019	M	L	L	L	Moderate
Park et al. [28]	2016	M	M	L	M	High
Grudet et al. [26]	2014	M	L	M	L	Moderate
John C. Umhau et al. [25]	2013	M	M	L	L	Moderate

**Fig. 1** PRISMA flow diagram

Meta-analysis
Vitamin D deficiency and suicide attempt (Sensitivity analysis)

Out of 13 eligible studies, five articles [11–13, 21, 26] examined the relationship between vitamin D deficiency and the risk of suicide attempts (SA). Among these, one study [13] was identified as having the highest risk of bias. Figure 2 demonstrates the sensitivity analysis of the pooled association between vitamin D deficiency and the risk of SA, including all eligible articles (Fig. 2-A) and excluding one record with a high risk of bias (Fig. 2-B). In

both analyses (records including/excluding the high risk of bias), vitamin D deficiency non-significantly increased the likelihood of SA by 1.61 and 1.65 times, respectively (Fig. 2-A: pooled OR=1.61; 95% CI: 0.98 – 2.65; I²=85%), and (Fig. 2-B: pooled OR=1.65; 95% CI: 0.98 – 2.80; I²=91%).

Vitamin D deficiency and suicide and suicide ideation

Likewise, a meta-analysis of five studies using the random effects model demonstrated a non-significant association between vitamin D deficiency and the risk

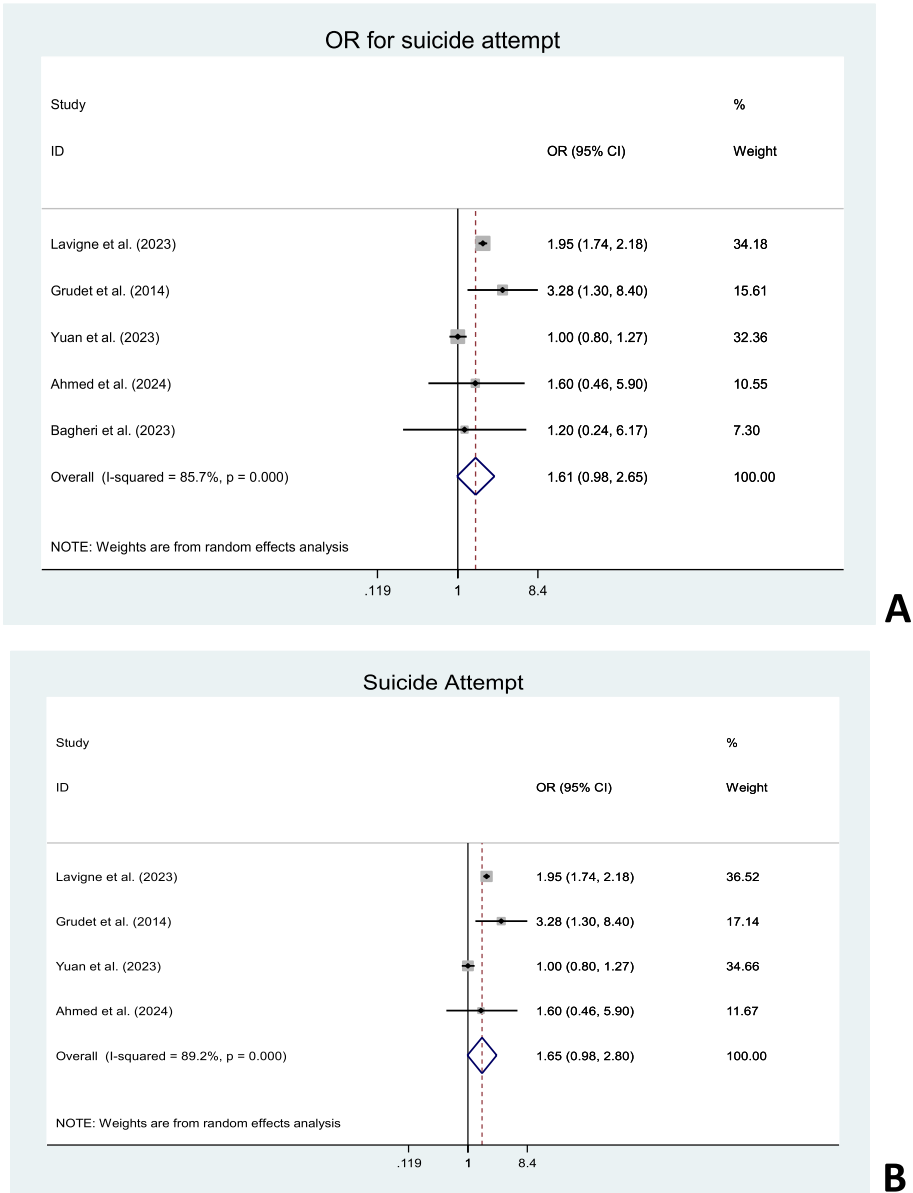


Fig. 2 Sensitivity analysis of pooled odds ratio for the association between vitamin D deficiency and the risk of suicide attempt (**A**=with all 5 records; **B**=after excluding one poor quality record). OR: odds ratio

of suicidal ideation (Pooled OR=1.15; 95% CI: 0.94 – 1.41; $I^2=92\%$) (Fig. 3). In Fig. 4, the pooled OR of suicide death was shown using a meta-analysis forest plot of three studies via the random effects model. We also found a positive association between vitamin deficiency and the risk of suicide by 1.7 times (Pooled OR=1.7; 95% CI: 0.93 – 3.12; $I^2=86\%$). However, this relationship was not statistically significant. Standard mean difference of vitamin D levels among suicidal patients.

Figure 5 shows the standard mean difference (SMD) of vitamin D blood serum levels between control subjects and patients with SBs. Meta-analysis of 9 studies [12, 20, 25, 26, 28–32] using SMD and the random effects model revealed significantly lower serum levels of vitamin D in patients with SBs than controls without any SBs (SMD= - 0.69; 95% CI: - 0.89 – - 0.49). Conversely, the study found a significant difference in vitamin D levels between suicidal patients and individuals without any suicidal behaviors.

Discussion

The current meta-analysis is among the few review studies that assessed the relationship between vitamin D deficiency and SBs. This meta-analysis yielded the pooled odds ratios for the risk of suicide, suicide attempts (SA), and suicidal ideation (SI) in individuals with vitamin D deficiency. Additionally, we estimated the standardized mean difference (SMD) in serum vitamin D levels between the groups with and without SBs using a random effects model meta-analysis.

The results of the analysis showed that vitamin D deficiency was associated with an increased risk of suicide, SA, and SI, while the strength and the measure of associations are not very strong. This meta-analysis included 13 eligible studies, most of which compared serum vitamin D levels between groups with and without suicidal behavior, revealing a significant difference in mean vitamin D levels.

However, regarding the strengths and weaknesses of the included studies, nine studies [12, 20, 25, 26, 28–31] measured the quantitative (continuous) value of vitamin D levels. Regarding various suicidal behaviors, five

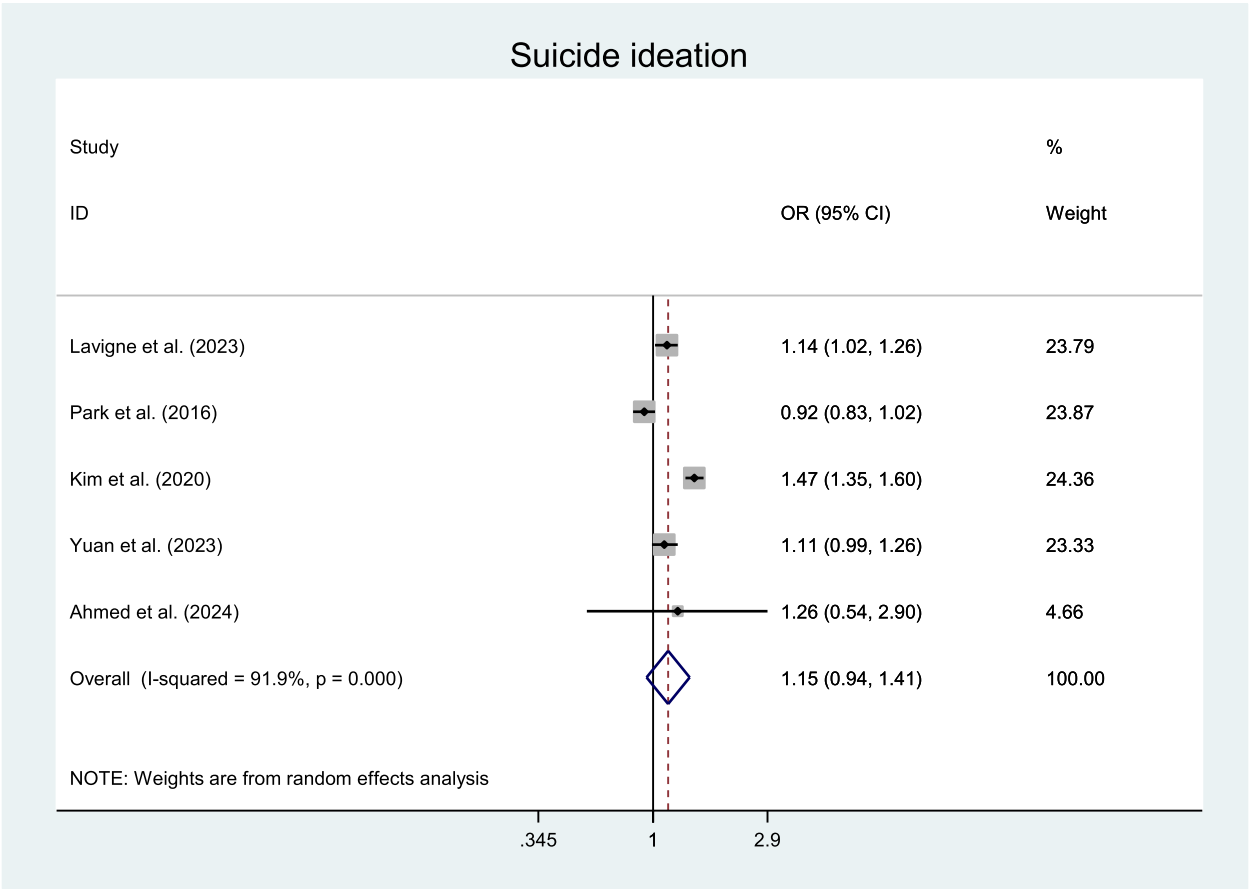


Fig. 3 Meta-analysis of the association between vitamin D deficiency and suicide ideation

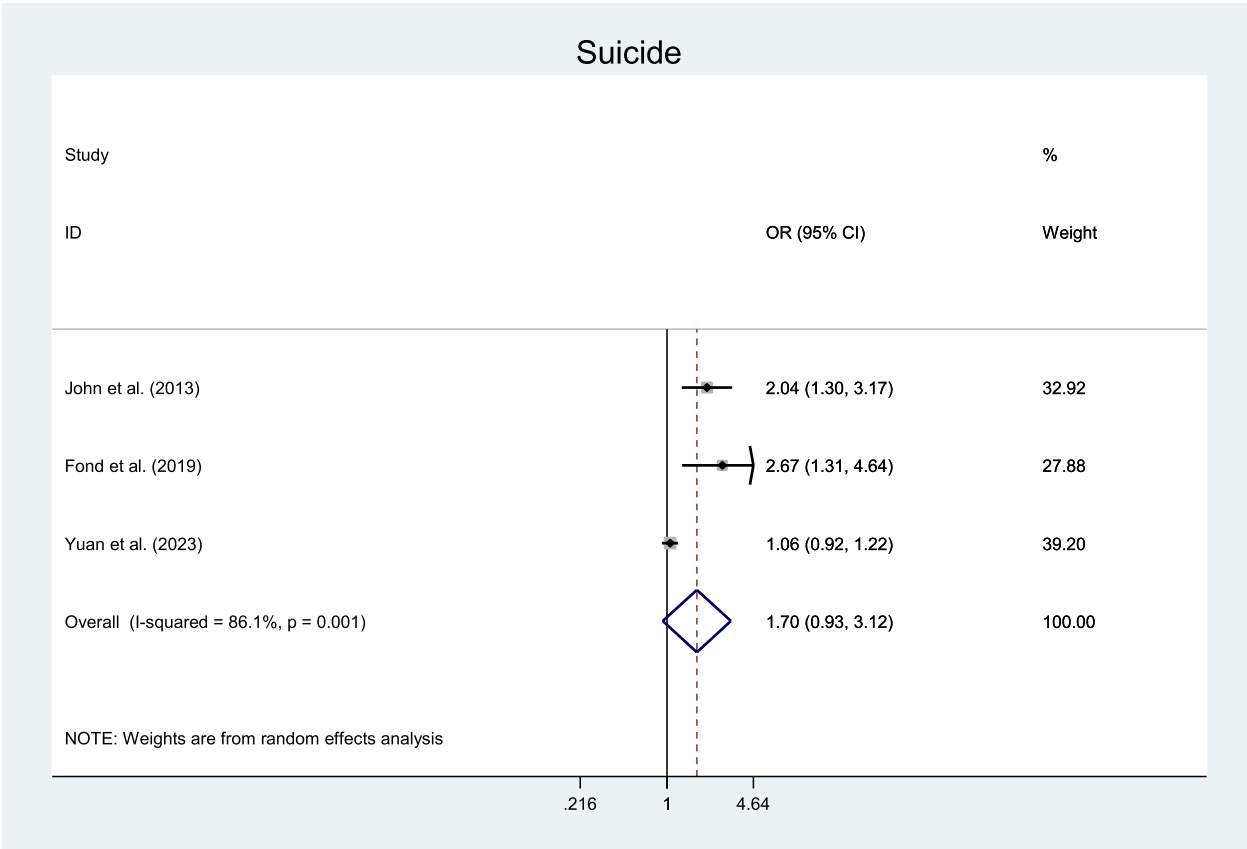


Fig. 4 Meta-analysis of the association between vitamin D deficiency and the risk of suicide

studies [11–13, 21, 26] assessed the frequency of suicide attempts, five studies examined the frequency of suicidal ideation [11, 12, 20, 21, 28], and three studies analyzed the frequency of suicide (death) [11, 25, 27] in comparison to the control group. Providing appropriate effect sizes such as odds ratio and relative risk can lead to a better understanding of the relationship between suicidal behaviors and vitamin D levels. Furthermore, one study had a high risk of bias in the quality assessment [13]. To address this issue, the review used sensitivity analysis. Among the eligible studies in the review, almost all of them identified low levels of vitamin D in relation to the risk of suicidal behaviors. Vitamin D supplementation reduced the risk of suicide attempts among veterans in the USA [21] and in the cadre members of the military [25]. This shows a significant relationship between vitamin D deficiency and suicide risk. Agoraphobic patients suffering from vitamin D deficiency have taken vitamin D supplements to reduce SBs [27]. Additionally, suicidal tendencies increased among depressive disorder patients with vitamin D deficiency [12, 31]. Furthermore, lower vitamin D was associated with indices of immune activation in major depressive disorders [29]. Another included

study has identified vitamin D deficiency as a significant risk factor for suicide in teenagers, suggesting that physicians should take vitamin D levels into account during routine examinations [32]. Moreover, one of the included studies indicated that vitamin D deficiency could be a contributing factor to the elevated pro-inflammatory cytokines [26]. However, a significant association between SBs and low levels of vitamin D was not seen within the included studies [11, 25, 29]. This level of attributable risk for vitamin D deficiency can be highly effective in suicide prevention programs.

Another weakness in the included studies was the absence of risk estimation for suicide in individuals with vitamin D deficiency based on gender, as only one of the included studies provided this data [21]. For example, suicide and suicidal behavior among women of reproductive-age can lead to severe and dangerous consequences, particularly during the perinatal period and after delivery; vitamin D deficiency has a synergistic interaction effect with depression [33]. We also highlighted this issue among early married and adolescent pregnant girls in a case–control design [34]. We recommend that prospective cohort studies be conducted with a more thorough

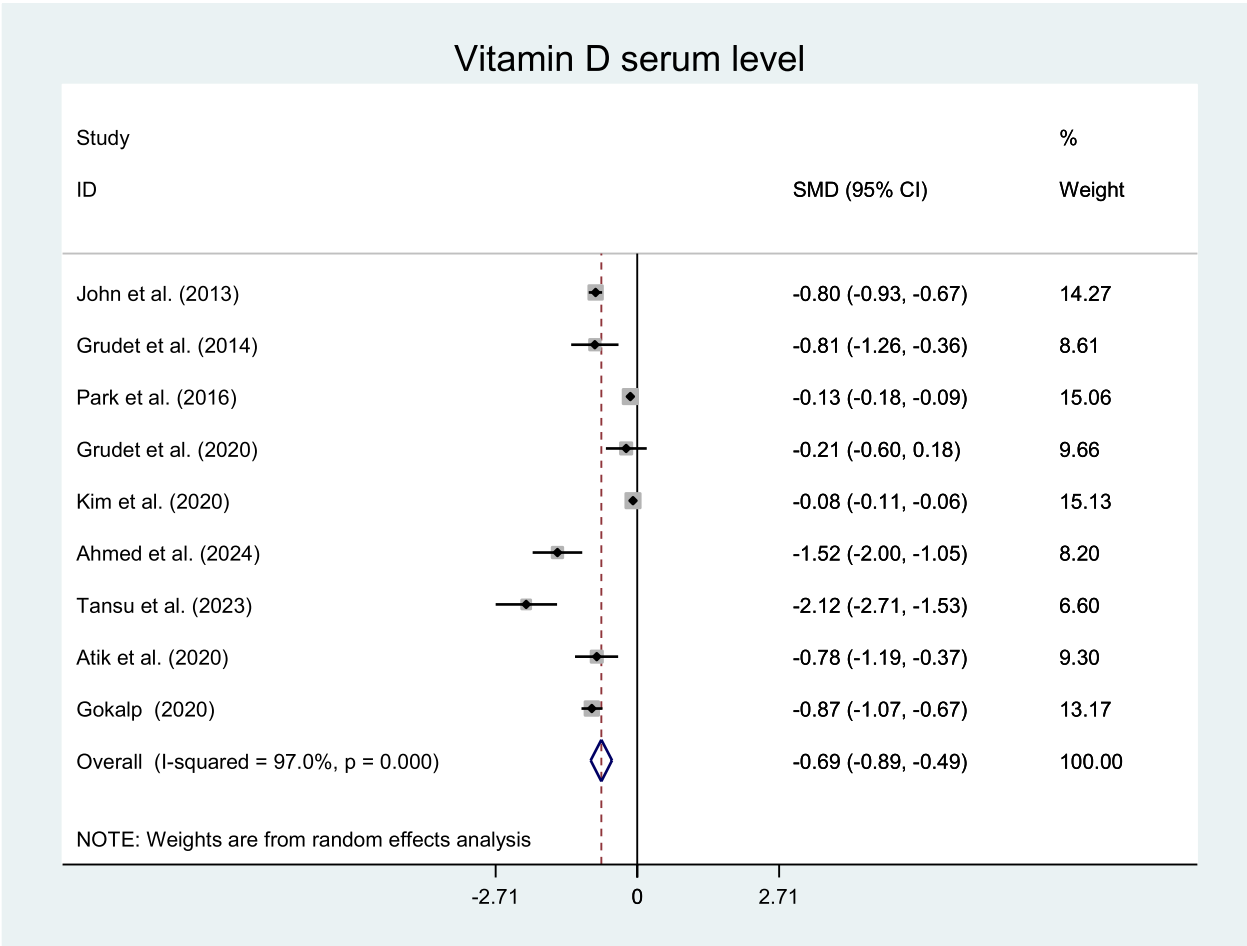


Fig. 5 Meta-analysis of the standard mean difference (SMD) of vitamin D blood serum level between healthy people and patients with suicidal behaviors

analysis. Additionally, we suggest that the severity of vitamin D deficiency and the duration of exposure for patients with this deficiency be taken into account in cohort and/or longitudinal designs.

During the review, it was noted that the prevalence of vitamin D deficiency was 58% and levels of vitamin D were significantly lower than those in healthy controls and depressive patients without SBs [26]. It is evident that the low levels of vitamin D in plasma were associated with elevated inflammatory markers in psychiatric patients (specifically IL-1 β and IL-6). As we and others have previously shown that peripheral and central inflammation is increased in suicidal patients, it seems that low levels of vitamin D could be a contributing cause of this inflammation. As inflammation is suggested to be directly part of the neural mechanisms underlying depressive and suicidal behavior, it should be of high relevance to detect and cure vitamin D deficiency in these patients [26]. However, a positive

relationship between vitamin D deficiency and suicidal behaviors has not been statistically significant [11–13].

Among all micronutrient deficiencies, vitamin D deficiency is now considered an epidemic. According to global estimates, more than 1 billion people are known to be vitamin D deficient, an issue of considerable importance in the twenty-first century [35, 36]. It is important to note that variations in sunlight exposure can lead to fluctuations in vitamin D levels. Engaging in both indoor and outdoor activities can contribute to these variations and may result in a decrease in vitamin D levels [37]. Currently, a meta-analysis indicates that outdoor training is associated with a slightly higher vitamin D concentration. However, vitamin D levels are significantly influenced by the season. This review suggested that working outdoors alone is insufficient to ensure adequate vitamin D levels [38]. Additionally, another study found that winter negatively affects vitamin D levels among athletes [39].

Vitamin D deficiency may increase the risk of suicide and SBs in several pathways. It has been shown that vitamin D deficiency has been linked to symptoms resembling depression, such as fatigue, mood alterations, suicidal thoughts, anxiety, changes in appetite and weight, insomnia, and forgetfulness [40]. Evidence indicated that low serum vitamin D levels are linked to various mental and physical disorders, especially depression and affective disorders. In fact, vitamin D deficiency can lead to suicide and suicidal behaviors through these pathways, particularly depression and mood changes [31, 41].

Limitations

The current meta-analysis found that lower levels of vitamin D are linked to an increased risk of suicide, suicidal attempts (SA), and suicidal ideation (SI). However, our study had several limitations. There was significant heterogeneity among the studies. One reason for this was the limited number of eligible studies could effect on the statistical power. Additionally, the eligible studies targeted different study groups, making it possible that the severity of vitamin D deficiency and the risk of suicide vary among these sub-populations. Furthermore, most studies compared vitamin D serum levels as a quantitative variable across study groups, and many did not utilize effect sizes such as odds ratios (OR) and relative risks (RR) to assess the strength of the association between vitamin D deficiency and suicide or suicidal behaviors.

Nonetheless, this meta-analysis is one of the few that has revealed and analyzed the relationship between vitamin D deficiency and suicidal behaviors (suicide, SA, and SI) using a quantitative pooled estimate (SMD) and a reliable effect size (pooled odds ratio) with 95% CIs.

Conclusions

The results of this meta-analysis indicated that serum levels of vitamin D are lower in patients with SBs, and vitamin D deficiency non-significantly increased the risk of suicide, attempted suicide, and suicidal ideation. These findings can inform suicide prevention programs, particularly for target groups experiencing significant vitamin D deficiency.

Longitudinal and prospective cohort studies with more in-depth and sex-based analyses involving pregnant and postpartum women are recommended for a more comprehensive and true understanding of the relationship between vitamin D deficiency and suicide.

Appendix

PubMed search strategy

((((((((((suicide[Title/Abstract]) OR (suicide attempt[Title/Abstract])) OR (suicidal behavior*[Title/

Abstract])) OR (suicide ideation[Title/Abstract])) OR (self-harm[Title/Abstract])) OR (completed suicide[Title/Abstract])) OR (mental disorder[Title/Abstract])) OR (Mental Illness[Title/Abstract])) OR (psychiatric[Title/Abstract])) OR (depression[Title/Abstract])) AND (vitamin D[Title/Abstract])) OR (Vitamin D Deficiency[Title/Abstract])) OR (25-Hydroxyvitamin[Title/Abstract])).

Abbreviations

SA	Suicide attempt
SI	Suicidal ideation
CI	Confidence interval
OR	Odds ratio
RR	Relative risk
SMD	Standard mean difference

Acknowledgements

Authors would like to thank the statistical and epidemiological supports of "Clinical Research Development Unit of Al-Zahra Hospital", at Tabriz University of Medical Sciences.

Clinical trial number

Not applicable.

Authors' contributions

HA and JY developed the original idea and contributed to the protocol development, reviewed the first draft of the manuscript, and interpreted and revised the results. HA, SNM, and LGK contributed to the protocol development, conducted, search, analyzed, and provided the first draft of the manuscript. JSM, SVM, MK, IS, MSJ, and BH contributed to the protocol development, records screening, data extraction, review, and technical comments. All authors reviewed and approved the final draft of the manuscript.

Funding

This meta-analysis was funded by Tabriz University of Medical Sciences.

Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by "Central Ethics Committee of Tabriz university of Medical Sciences" (Ethic number: IR.TBZMED.REC.1402.760). Authors confirm that all procedures were carried out in accordance with relevant guidelines and regulations.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Received: 4 November 2024 Accepted: 14 February 2025

Published online: 26 February 2025

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