Review Article

Association between Vitamin D Deficiency and Insulin Resistance in Type 2 Diabetic Adult Patients: Systematic Review

Saud S. Alharbi[1], Manar S. Alfaqiri[2], Najla K. Alanazi[2], Arwa F. Alanazi[2], Rand F. Albaridi[2], Hatem H. Alquthami[2], Riymaz J. Aljohani[2], Rana H. Alqarni[2], Sarah T. Alnajim[2], Alaa M. Althobiti[2], Ashwaq A. Albalawi[2], Mohammed M. Alqahtani[2], Hassan A. Alhwiti[2], Waad S. Albalawi[3]

[1]Consultant Family Medicine, Assistant Professor Family Medicine, Department of Family and Community Medicine, Faculty of Medicine, University of Tabuk, Tabuk, KSA.

[2] Medical Intern, Faculty of Medicine, University of Tabuk, Tabuk, KSA.

[3] General Practitioner, General Hospital of Tayma, Tabuk, KSA.

ABSTRACT

The recognized biomarker of vitamin D status have been repeatedly linked to an increased risk of insulin resistance, metabolic syndrome, and the subsequent development of type 2 diabetes, according to an increasing body of epidemiological evidence. This systematic review aimed to investigate the relationship between vitamin D deficiency and insulin resistance (IR) in adults with Type 2 Diabetes Mellitus (T2DM). It highlights a consistent inverse association between vitamin D levels and IR, but the efficacy of vitamin D supplementation in improving IR remains inconsistent across various interventional studies. The review followed PRISMA guidelines and included a systematic search of studies in multiple databases, yielding 13 studies with 1,396 participants. Most observational studies (8 of 11) showed a significant inverse correlation between serum 25-hydroxyvitamin D and HOMA-IR. However, interventional studies produced conflicting results; one randomized controlled trial (RCT) indicated improvement in HOMA-IR with high-dose vitamin D supplementation, while others found no effect. The overall evidence quality was deemed low, with a high risk of bias attributed to the lack of control for confounders like body mass index (BMI) and physical activity. Despite the consistent reporting of an inverse relationship in observational studies, interventional data do not support a causal link. The inconsistency across studies may reflect confounding by BMI, sunlight exposure, and physical activity. Consequently, current evidence does not strongly advocate for vitamin D supplementation as an isolated treatment for improving insulin resistance in T2DM, underlining the necessity for more rigorous clinical trials.

Keyword: Vitamin D Deficiency, Insulin Resistance, Type 2 Diabetes Mellitus, 25-Hydroxyvitamin D, HOMA-IR, Systematic Review.

Introduction

Type 2 One of the most important worldwide health issues of the twenty-first century is diabetes mellitus (T2DM), characterized by a escalating prevalence that places an immense burden on healthcare systems and economies worldwide. This metabolic disorder is fundamentally underpinned by two core pathophysiological defects: Insulin resistance (IR) is a syndrome marked by a gradual loss in pancreatic β-cell activity and, more importantly, diminished insulin sensitivity in peripheral tissues [1].

Access this article online	
Quick Response Code:	Website: www.smh-j.com
	DOI: 10.54293/smhj.v6i1.176

Address for correspondence: Saud Salman Alharbi, Consultant Family Medicine, Assistant Professor Family Medicine, Department of Family and Community Medicine, Faculty of Medicine, University of Tabuk, Tabuk, KSA.

E-mail: Salrehily@ut.edu.sa

Received: 21 Sep 2025 **Accepted:** 8 Nov 2025

Please cite this article as: Salman Alharbi S, Alfaqiri MSA, Alanazi NKA, Alanazi AFN, Albaridi RFM, Alquthami HHM, Aljohani RJM, Alqarni RHS, Alnajim STA, Althobiti AMF, Albalawi AAM, Alqahtani MMH, Alhwiti HAH, ALBalawi WSO. Association between Vitamin D Deficiency and Insulin Resistance in Type 2 Diabetic Adult Patients: Systematic Review. SMHJ [Internet]. 2025;6(1):119-130.

Insulin resistance is not merely a precursor but a central driver of T2DM, contributing to hyperglycemia and fostering the development of its devastating macrovascular and microvascular complications, including cardiovascular disease, nephropathy, retinopathy, and neuropathy [2]. The intricate mechanisms behind IR are multifactorial, involving a complex interplay of genetic predisposition, obesity, physical inactivity, and chronic low-grade inflammation. In parallel, vitamin D deficiency has emerged as another highly prevalent nutritional deficiency with widespread implications for public health, affecting an estimated one billion people globally across all age groups and ethnicities [3]. Now known as a powerful secosteroid hormone with a wide range of pleiotropic effects, vitamin D was initially recognized for its role in calcium–phosphate homeostasis in controlling calcium-phosphate balance and bone mineralization. Vitamin D Receptors (VDR) were discovered, and the enzyme 1α-hydroxylase was expressed, required for vitamin D activation, in a vast array of extra-skeletal tissues—including pancreatic beta cells, skeletal muscle, and adipocytes—has unveiled its potential role in modulating metabolic processes, immune function, and cell proliferation [4]. This broad expression pattern provides a compelling biological plausibility for vitamin D's involvement in glucose metabolism and insulin action. Low circulating levels of 25-hydroxyvitamin D (25(OH)D), the recognized biomarker of vitamin D status, have been repeatedly linked to an increased risk of insulin resistance, metabolic syndrome, and the subsequent development of type 2 diabetes, according to an increasing body of epidemiological evidence [5, 6]. For instance, among US people without diabetes, a comprehensive cross-sectional study of data from the National Health and Nutrition Examination Survey (NHANES) clearly demonstrated a negative correlation between blood 25(OH)D concentrations and the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) [7]. Many different processes have been proposed to explain this connection. By directly promoting the development of insulin receptors in target tissues, vitamin D is thought to improve insulin sensitivity. facilitating insulin-mediated glucose transport, and modulating intracellular calcium flux, which is a critical second messenger for insulin action within cells [4]. Additionally, pro-inflammatory cytokines like TNF-α and IL-6, which are known to disrupt insulin signaling pathways and encourage IR, are suppressed by vitamin D, which has strong anti-inflammatory properties [8]. It may also influence insulin secretion by interacting with VDRs on pancreatic beta-cells. The results of interventional studies examining the causal role of vitamin D supplementation in enhancing insulin sensitivity in diabetic and pre-diabetic populations have been notably inconsistent and frequently disappointing, despite this strong observational association and supporting mechanistic data. Vitamin D supplementation has been shown to enhance IR parameters in certain randomized controlled trials (RCTs), but not in others, including a number of large-scale, carefully planned experiments [5, 6]. This discrepancy highlights a critical gap in knowledge and suggests that the relationship may be confounded by other factors or may only be relevant in specific subpopulations. The existing systematic reviews on this topic often encompass broad populations, including prediabetics, healthy individuals, and those with metabolic syndrome, which may dilute the specific effect in a dedicated T2DM cohort. There remains a pressing need to synthesize and critically appraise the current evidence specifically focused on the adult T2DM population, where the clinical implications of mitigating insulin resistance are most direct and significant. Study Objective: Thus, this systematic review's main goal is to thoroughly assess and compile the available data about the link between vitamin D insufficiency and insulin resistance, particularly in adult patients with Type 2 Diabetes Mellitus.

Methods

To guarantee a clear and thorough reporting of the methods and results, this systematic review was carried out strictly in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria [9]. Several important electronic bibliographic databases, including PubMed/MEDLINE, Web of Science Core Collection, Scopus, and ScienceDirect, were searched using a methodical and thorough approach. The purpose of the search was to find any pertinent published research examining the relationship between insulin resistance and vitamin D insufficiency in adult patients diagnosed with Type 2 Diabetes Mellitus (T2DM). To increase the search sensitivity and specificity, a mix of free-text keywords associated with the fundamental ideas of "Vitamin D," "Insulin Resistance," and "Type 2 Diabetes Mellitus" as well as controlled vocabulary terms like Medical Subject Headings (MeSH) were used in conjunction with Boolean operators. Only English-language publications were included in the search. Eligibility Criteria: The study selection process

was governed by pre-defined eligibility criteria. Adult human patients (18 years of age and older) having a verified diagnosis of Type 2 Diabetes Mellitus comprised the population of interest. Vitamin D deficit or insufficiency, as determined by blood 25-hydroxyvitamin D (25(OH)D) levels, was the exposure. Insulin resistance was the result of interest, as determined by validated indices such the hyperinsulinemic-euglycemic clamp, the quantitative insulin sensitivity check index (QUICKI), the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), or other established biomarkers. In order to examine this connection, we considered observational research like cohort, case-control, and cross-sectional studies as well as interventional studies like randomized controlled trials (RCTs) and non-randomized trials. Excluded from consideration were review articles, editorials, comments, letters to the editor, case reports, abstracts from conferences, and research done in vitro or on animals. Excluded studies were also those without original data or those without full text accessible. Data Extraction: To reduce bias and guarantee consistency, two reviewers separately carried out the full research selection procedure. Initially, all identified records were imported into the Rayyan QCRI web application for systematic reviews [10] for the purpose of deduplication. After that, the remaining unique citations' titles and abstracts were checked against the qualifying requirements. Studies that were deemed potentially relevant by either reviewer were advanced to the full-text assessment stage. Both reviewers separately downloaded and thoroughly assessed the complete texts of these papers. Discussions or, if required, contact with a third reviewer were used to settle any disputes that surfaced throughout the selection process. A pre-piloted, standardized data extraction form was used to obtain data from all studies that satisfied the inclusion criteria. Included in the retrieved data were: first author, year of publication, nation of origin, study design, sample size, participant characteristics (e.g., mean age, gender distribution, BMI, duration of diabetes), techniques for measuring vitamin D status and insulin resistance, key findings (including statistical significance and measures of association), and the authors' primary conclusions. Data Synthesis Strategy: The results from the included research were compiled and presented using a narrative synthesis technique. Given the anticipated heterogeneity in study designs, populations, interventions (for RCTs), and methods used to measure both exposure and outcome, a meta-analysis was deemed inappropriate. To give a clear and succinct review of the study's features and the main findings on the connection between vitamin D and insulin resistance, the data are displayed in organized summary tables. The tables organize the evidence by study design and highlight the direction and strength of the reported associations, allowing for a comparative analysis of the findings across different settings and methodologies. Risk of Bias Assessment: Two independent reviewers used suitable, proven techniques to objectively evaluate the included studies' methodological quality and danger of bias. The Cochrane Risk of Bias 2 (RoB 2) tool was used for randomized controlled trials [11]. Cohort, case-control, and cross-sectional designs were among the observational studies for which the Joanna Briggs Institute (JBI) critical evaluation checklists were used. An overall assessment of the risk of bias (low, moderate, or high) was established after each study was compared to the particular domains of the corresponding instrument. A clear assessment of the reliability and validity of the evidence base is provided by the summary table that contains the assessment's findings.

Results

(Figure 1) illustrates the systematic process of study selection for a literature review, beginning with 1,211 records identified from databases. After removing 598 duplicates, 613 records were screened, resulting in 214 exclusions. Of the 399 records sought for retrieval, 278 were not retrieved, leaving 121 to be assessed for eligibility. Following the exclusion of 108 records due to wrong outcomes, wrong population, or being abstracts only, 13 more studies were added to the review. This systematic review comprises thirteen papers [12- 24], as detailed in (Table 1), exhibit considerable diversity in their geographical and methodological approaches, giving a comprehensive overview of the relationship between insulin resistance (IR) and vitamin D in Type 2 Diabetes Mellitus (T2DM). The research was conducted across ten different countries, with a notable concentration in Asia (China [15, 16, 19, 21, 23], Iran [12], Iraq [13, 18], Yemen [20], Indonesia [22], and India [24]) and Africa (Nigeria [14] and Kenya [8]). The study designs were varied, encompassing observational methods—including cross-sectional [13, 14, 17, 18, 20, 23, 24], case-control [13, 24], and retrospective cohort [21] studies—as well as interventional trials, such as pre-post studies [12] and randomized controlled trials (RCTs) [16, 22]. The total sample size across all studies was 1,396 adults with T2DM, with individual study sizes ranging from 40 [12] to 172 [23]

participants. A critical observation from (Table 1) is the frequent lack of reporting regarding the specific assay used to measure serum 25-hydroxyvitamin D levels, a key methodological detail. Eleven research employed the Homeostatic Model Assessment (HOMA-IR), the main instrument for evaluating insulin resistance [13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 24], while one study used a calculated Insulin Resistance Index [23] and another used the Leptin-to-Adiponectin Ratio (LAR) [12]. The synthesized findings from these studies, presented in (Table 2), reveal a complex and often contradictory relationship between vitamin D status and IR in T2DM. A majority of the observational studies reported a significant inverse association, suggesting that lower vitamin D levels are linked to higher HOMA-IR values. For instance, Adeleye et al. [14] found a significant negative correlation, Zhang et al. [15] reported a negative β-coefficient, and Gao & Chen [19] as well as Al-Shami et al. [20] concluded that vitamin D deficiency was associated with significantly worse IR. This relationship was further supported by studies identifying low vitamin D as an independent risk factor for IR [21, 23]. However, this consensus is not universal. The study by Said et al. [8] In a Kenyan sample, Prasad et al.'s case-control research revealed no association between vitamin D and HOMA-IR [24] discovered no discernible change in HOMA-IR between T2DM patients with and without vitamin D deficiency. The results from interventional studies add another layer of complexity. Alvina et al. [22] demonstrated that high-dose vitamin D supplementation over six months led to a significant improvement in HOMA-IR compared to placebo. In contrast, Gharekhani et al. [12] found that correcting vitamin D deficiency had no effect on their chosen IR marker (LAR), and Sun et al. [16] reported that a combined exercise and vitamin D intervention failed to improve HOMA-IR, attributing this to high inter-individual variability. As shown in (Table 2), reflect this dichotomy. Numerous studies provide compelling evidence that vitamin D plays a part in regulating insulin sensitivity, proposing it as a surrogate marker for IR [14] or a therapeutic target to improve metabolic parameters [19, 21, 22]. Conversely, other studies conclude that there is no evident causal relationship [12, 17, 24] or highlight the confounding influence of significant variability in patient response [16]. This inconsistency can be attributed to several factors evident in the tables, including the use of different biomarkers for IR (HOMA-IR vs. LAR), varying degrees of adjustment for powerful confounders like BMI, and the diverse baseline characteristics of the studied populations across different ethnicities and regions.

Discussion

The results of this systematic review summarized data from thirteen studies examining the relationship between insulin resistance (IR) and vitamin D insufficiency in adult patients with Type 2 Diabetes Mellitus (T2DM), present a complex and nuanced picture. The collective results indicate a frequently observed inverse epidemiological association; however, interventional data remain inconsistent, and the overall body of evidence is constrained by a high risk of bias. This discussion will contextualize these findings within the broader existing literature, explore potential mechanisms, acknowledge the significant limitations of the current evidence, and propose directions for future research. Our analysis's main conclusion is that most of the included observational studies found a statistically significant inverse relationship between HOMA-IR values and blood 25-hydroxyvitamin D [25(OH)D] levels [14, 15, 19, 20, 23]. This aligns consistently with a substantial body of previous cross-sectional research conducted in various populations. For instance, a large analysis of NHANES data demonstrated a significant inverse association between 25(OH)D and HOMA-IR among non-diabetic US adults, though this relationship was absent in non-Hispanic Blacks after full adjustment for confounders [25]. Similarly, despite a shocking 100% incidence of vitamin D insufficiency, Ehrampoush et al. (2021) discovered a substantial negative connection between vitamin D levels and multiple IR indicators (FPG, insulin, HOMA2-IR) in a large Iranian cohort from a nutrition clinic [26]. Our findings in T2DM populations, such as those in Nigeria [14] and China [15, 19], extend this observed association to a demographic already characterized by significant metabolic dysregulation. It is important to acknowledge that the cross-sectional nature of these studies limits causal inference, as reverse causality—whereby insulin resistance or its associated lifestyle factors could lead to lower vitamin D levels—cannot be ruled out. The biological plausibility for this link is strong. The skeletal muscle, adipose tissue, and beta-cells in the pancreas all express vitamin D receptors (VDR). Vitamin D's active form, 1,25-dihydroxyvitamin D, is thought to affect insulin sensitivity by binding to these VDRs and altering the expression of genes involved in insulin signaling, such as the insulin receptor [27]. Proposed mechanisms include the reduction of chronic low-grade

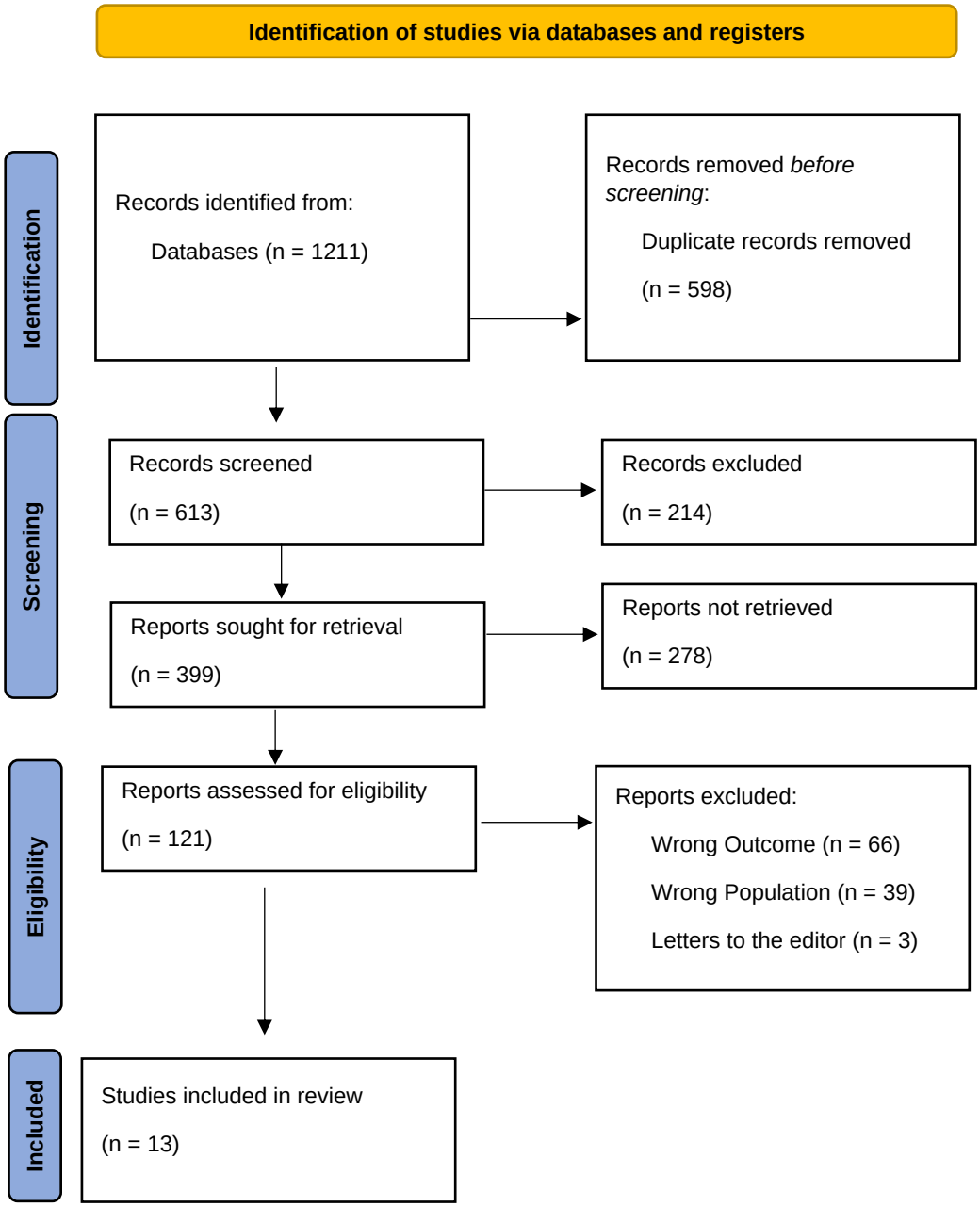

Figure 1: PRISMA Flow Diagram of Study Selection Process.

Table 1: Characteristics of the Included Studies.

Study Author(s) & Year [Ref]	Country	Study Design	Sample Size (T2DM only)	Participant Characteristics (T2DM Group)	Vitamin D Measurement	Insulin Resistance Measurement
Gharekhani et al., 2020 [12]	Iran	Interventional (Pre-Post)	40	Adults with T2DM and Vit D deficiency/insufficiency	Chemiluminescent Microparticle Immunoassay (CMIA)	Leptin-to-Adiponectin Ratio (LAR)
Arif & Rasheed, 2024 [13]	Iraq	Case-Control	150 (Cases)	Male adults with T2DM (some with CAD)	NR	HOMA-IR
Adeleye et al., 2023 [14]	Nigeria	Comparative Cross-sectional	120	Adults with T2DM	NR	HOMA-IR
Zhang et al., 2021 [15]	China	Retrospective Cross-sectional	109	Non-osteoporosis adults with T2DM	NR	HOMA-IR
Sun et al., 2023 [16]	China	Randomized Controlled Trial (RCT)	61	Middle-aged adults with T2DM	NR	HOMA-IR (Primary outcome)
Said et al., 2021 [17]	Kenya	Cross-sectional	124	Adults with T2DM (not on insulin/thiazolidinediones)	NR	HOMA-IR, Disposition Index
Hashim & Qasim, 2022 [18]	Iraq	Cross-sectional	100	Adults with T2DM	NR	HOMA-IR, HOMA-B
Gao & Chen, 2022 [19]	China	Comparative (Cross-sectional)	80	Elderly (Senile) adults with T2DM	NR	HOMA-IR
Al-Shami et al., 2025 [20]	Yemen	Cross-sectional	50 (Cases)	Adults with T2DM (aged 23-65 years)	NR	HOMA-IR, HOMA-B
Sun et al., 2023 [21]	China	Retrospective Cohort	100 (Resistance group)	Adults with T2DM and Insulin Resistance	NR	HOMA-IR
Alvina et al., 2023 [22]	Indonesia	Randomized Controlled Trial (RCT)	94 (47 in Vit D arm)	Adults with T2DM (duration ≤3 years)	NR	HOMA-IR
Zhao et al., 2021 [23]	China	Cross-sectional	172	Adults with T2DM (mean age 53.2±10.6)	NR	IR Index (20/[C-peptide × FPG])

Prasad et al., 2022 [24]	India	Case-Control	92 (Cases)	Adults with T2DM	NR	HOMA-IR, HOMA-B

Abbreviations: NR: Not reported in the provided abstract; T2DM: Type 2 Diabetes Mellitus; HOMA-IR: Homeostatic Model Assessment of Insulin Resistance; HOMA-B: Homeostatic Model Assessment of β-cell function; CAD: Coronary Artery Disease; RCT: Randomized Controlled Trial.

Table 2: Key Findings on Vitamin D and Insulin Resistance in T2DM.

Study Author(s) & Year [Ref]	Key Findings on Vitamin D Status	Key Findings on Association/Intervention	Main Conclusion
Gharekhani et al., 2020 [12]	Deficiency/Insufficiency (Inclusion criteria)	Treatment of Vit D deficiency did not change LAR (a marker of IR).	Vit D treatment did not change insulin resistance in T2DM patients.
Arif & Rasheed, 2024 [13]	Levels significantly lower in T2DM groups vs. controls.	All diabetic patients had insulin resistance. Increased HbA1c, insulin, HOMA-IR associated with CAD progression.	Vitamin D deficiency may contribute to insulin resistance in male T2DM patients.
Adeleye et al., 2023 [14]	Mean level significantly lower in T2DM vs. controls (35.84 vs. 44.71 ng/mL).	Significant negative correlation between serum Vit D and HOMA-IR. Mean Vit D higher in patients with HOMA-IR <2.	Vitamin D levels may be used as a surrogate marker of IR.
Zhang et al., 2021 [15]	25(OH)D negatively correlated with HOMA-IR (β = -0.349).	25(OH)D negatively correlated with bone turnover marker (BALP) and HOMA-IR, positively with IGF-1.	25(OH)D concentrations are negatively correlated with insulin resistance and bone turnover.
Sun et al., 2023 [16]	NR	The intervention (exercise ± Vit D) failed to improve HOMA-IR. High inter-individual variability was observed.	The combined intervention did not improve HOMA-IR, likely due to large inter-individual variability.
Said et al., 2021 [17]	71.1% of participants were deficient.	Vitamin D levels showed a low positive correlation with Disposition Index (beta cell function) but not with HOMA-IR.	Vitamin D deficiency is prevalent but was not correlated with HOMA-IR in this cohort.
Hashim & Qasim, 2022 [18]	NR	High Vit D level linked to lower HOMA-IR. Calcium positively connected with FBS, negatively with HOMA-B.	Vitamin D deficiency influences glycemic dysregulation. Disrupted calcium

			homeostasis may play a role in T2DM.
Gao & Chen, 2022 [19]	Group with deficiency had significantly lower levels.	Vit D deficiency group had significantly higher HOMA-IR and lower BMD & muscle mass. Negative correlation between 25(OH)D and HOMA-IR.	Higher serum Vit D may improve insulin resistance, limb muscle mass, and bone density.
Al-Shami et al., 2025 [20]	40% prevalence of deficiency in T2DM vs. 20% in controls.	Significant association between low Vit D levels and higher HOMA-IR and HOMA-B.	Vitamin D deficiency in T2DM may lead to increased insulin resistance.
Sun et al., 2023 [21]	Lower 25(OH)D-3 level in resistance group.	BMI, TG, HDL-C, **25(OH)D-3**, 2hPG, HbA1c were risk factors for IR. Vit D supplementation improved glucose/lipid metabolism in IR group.	25(OH)D-3 is an independent risk factor for IR. Supplementation improves metabolism in T2DM with IR.
Alvina et al., 2023 [22]	Level increased from 12.50 to 43.57 ng/mL after 3 months.	Vit D group showed improvement in HOMA-IR and insulin at 3 & 6 months compared to control. No change in FBG/HbA1c.	Vit D supplementation for 3/6 months improves HOMA-IR but not FBG/HbA1c.
Zhao et al., 2021 [23]	NR	After adjusting for all confounders, the IR index increased by 5.6% for every 1 ng/mL increase in 25OHD.	Vitamin D status is independently associated with IR in patients with T2DM.
Prasad et al., 2022 [24]	78.2% deficiency in T2DM vs. 64.1% in controls (NS).	No significant difference in HOMA-B or HOMA-IR between Vit D deficient and non-deficient T2DM groups.	No association between Vit D deficiency and insulin resistance or beta-cell function was found.

Abbreviations: LAR: Leptin-to-Adiponectin Ratio; NS: Not Statistically Significant; BALP: Bone Alkaline Phosphatase; IGF-1: Insulin-like Growth Factor 1; BMD: Bone Mineral Density.

Table 3: Risk of Bias Assessment for Included Studies Using Joanna Briggs Institute (JBI) Checklists**.**

Study Author(s) & Year [Ref]	**Study Design**	**JBI Checklist Used**	**Q 1**	**Q 2**	**Q 3**	**Q 4**	**Q 5**	**Q 6**	**Q 7**	**Q 8**	**Q9**	**Overall Risk of Bias**
Randomized Controlled Trials		**JBI for RCTs**										
Sun et al., 2023 [16]	RCT	(10 questions)	Y	Y	U	Y	Y	Y	Y	Y	Y	**Moderate**

Alvina et al., 2023 [22]	RCT	(10 questions)	Y	Y	U	Y	Y	Y	Y	Y	Y	**Moderate**
Quasi-Experimental Studies		**JBI for Quasi-Exp.**										
Gharekhani et al., 2020 [12]	Pre-Post	(9 questions)	Y	Y	N	Y	Y	Y	Y	Y	N/A	**High**
Analytical Cross-Sectional Studies		**JBI for Cross-Sectional**										
Adeleye et al., 2023 [14]	Cross-sectional	(8 questions)	U	Y	U	Y	N	Y	Y	Y	N/A	**High**
Zhang et al., 2021 [15]	Cross-sectional	(8 questions)	U	Y	U	Y	N	Y	Y	Y	N/A	**High**
Said et al., 2021 [17]	Cross-sectional	(8 questions)	U	Y	U	Y	N	Y	Y	Y	N/A	**High**
Hashim & Qasim, 2022 [18]	Cross-sectional	(8 questions)	U	Y	U	Y	N	Y	Y	Y	N/A	**High**
Gao & Chen, 2022 [19]	Cross-sectional	(8 questions)	U	Y	U	Y	N	Y	Y	Y	N/A	**High**
Zhao et al., 2021 [23]	Cross-sectional	(8 questions)	U	Y	U	Y	N	Y	Y	Y	N/A	**High**
Case-Control Studies		**JBI for Case-Control**										
Arif & Rasheed, 2024 [13]	Case-Control	(10 questions)	U	Y	U	Y	N	Y	Y	Y	Y	**High**
Prasad et al., 2022 [24]	Case-Control	(10 questions)	U	Y	U	Y	N	Y	Y	Y	Y	**High**
Cohort Studies		**JBI for Cohort**										
Sun et al., 2023 [21]	Retrospective Cohort	(11 questions)	U	Y	U	Y	N	Y	Y	Y	Y	**High**

Al-Shami et al., 2025 [20]	Cross-sectional*	(8 questions)	U	Y	U	Y	N	Y	Y	Y	N/A	**High**

inflammation and the regulation of intracellular calcium flux, which is essential for insulin-mediated intracellular processes. Furthermore, elevated levels of parathyroid hormone (PTH) have been associated with vitamin D insufficiency, which can itself promote insulin resistance [28], a mechanism observed in prediabetic populations [1]. However, the critical caveat from our review is that association does not equate to causation. The results from interventional studies, which provide a higher level of evidence, are markedly less consistent. While Alvina et al. (2023) reported that 5000 IU/day of vitamin D for 3-6 months significantly improved HOMA-IR in Indonesian T2DM patients compared to placebo [22], other trials failed to replicate this benefit. Gharekhani et al. (2020) found that treating vitamin D deficiency did not alter insulin resistance as measured by the leptin-to-adiponectin ratio (LAR) [12], and Sun et al. (2023) found that middle-aged Chinese T2DM patients' HOMA-IR was not improved by a combination endurance exercise and vitamin D supplementation intervention, citing high inter-individual variability as a key reason [16]. This inconsistency is mirrored in broader literature. A randomized placebo-controlled trial by Mirzaei-Azandaryani et al. (2022) on pregnant women with vitamin D insufficiency found that 4000 IU/day supplementation for 18 weeks did not affect HOMA-IR, fasting insulin, or the incidence of gestational diabetes [29]. Similarly, a study on obese, non-diabetic Brazilian women found that while lower vitamin D was correlated with higher HOMA-IR, the relationship was deeply confounded by adiposity [30]. A major RCT by Safwan et al. (2025) concluded that neither a low (600 IU/day) nor a high (3750 IU/day) dose of vitamin D over one year improved any insulin resistance indices (including HOMA-IR, TyG index, METS-IR) in overweight elderly individuals, most of whom had prediabetes [31]. This suggests that the observed association in observational studies may be significantly driven by confounding factors, such as obesity, sedentary lifestyle, and diet, which are linked to both low vitamin D status and insulin resistance, rather than by a direct therapeutic action of vitamin D. The role of confounding cannot be overstated and is the primary source of the high risk of bias identified in our assessment. The vast majority of the included observational studies [13, 14, 15, 17, 18, 19, 20, 21, 23, 24] failed to adequately identify or control for critical confounding variables. Body fat percentage, physical activity levels, sun exposure, and dietary patterns are all strong determinants of both vitamin D status and insulin sensitivity. The inability to control for these factors, as seen in the studies by Khan et al. (2021) on prediabetic adults where the association disappeared after analysis [1, 2], probably exaggerates how strongly vitamin D and IR are thought to be related. Furthermore, our review highlights significant demographic and ethnic variations. The study by Said et al. (2021) in a black Kenyan cohort found no correlation between vitamin D and HOMA-IR, instead identifying beta-cell dysfunction as the predominant defect [8]. This echoes the NHANES finding where the inverse association was not present in non-Hispanic Blacks [25] and suggests that genetic, lifestyle, or environmental factors may profoundly modify this relationship. Other effect modifiers were also identified in the literature. According to Tas et al. (2025), in obese teenagers, liver fat content and racial/ethnic background altered the relationship between changes in vitamin D status and HOMA-IR trajectories [32]. This indicates that the metabolic context, including comorbidities like NAFLD—which itself is tightly linked to IR [11]—can determine whether a vitamin D deficiency has a measurable impact on insulin sensitivity. Limitations: This systematic review has several important limitations. First, and most significantly, the risk of bias assessment concluded that the overall body of evidence is of low quality, primarily due to the observational nature of most studies and their nearly universal failure to account for key confounding factors like BMI, physical activity, and diet. Second,

our analysis relied on study abstracts rather than full texts, which inherently lack the methodological detail required for a full appraisal; the specific assays used to measure 25(OH)D were frequently not reported, introducing potential concerns about measurement validity and standardization across studies. Third, there was considerable heterogeneity in the studied populations (e.g., differing ethnicities, age ranges, diabetes durations), interventions (dose and duration of vitamin D supplementation), and methods used to assess insulin resistance (HOMA-IR vs. LAR), which limits the ability to perform a meaningful meta-analysis and draw unified conclusions due to heterogeneity. Finally, publication bias is a potential concern, as studies with null or negative findings are less likely to be published, which may have led to an overestimation of the association in the published literature.

Conclusion

While an inverse relationship between vitamin D deficiency and insulin resistance in Type 2 Diabetes Mellitus is observed, evidence from interventional studies is inconsistent and fails to support a direct therapeutic role for vitamin D supplementation. The association is likely influenced by shared factors such as adiposity, ethnicity, genetic background, and other metabolic conditions like NAFLD. Consequently, the use of vitamin D supplements for improving insulin resistance is not well supported. Future research should prioritize large-scale, long-term randomized controlled trials that account for confounding variables and target specific subpopulations that may benefit from supplementation. Until clearer evidence is available, attention should remain on established methods for enhancing insulin sensitivity like weight management, physical activity, and glycemic control.

Conflict of Interest

None

Funding

None

References

1. Williams A, Zhao S, Brock G, Kline D, Echouffo-Tcheugui JB, Effoe VS, et al. Vitamin D, parathyroid hormone, glucose metabolism and incident diabetes in the multiethnic study of atherosclerosis. BMJ Open Diabetes Res Care. 2022;10(5):e002931. doi:10.1136/bmjdrc-2022-002931
2. Khorasani ZM, Bonakdaran S, Rafieie HP. The Relationship Between Vitamin D Deficiency and Insulin Resistance in Pregnant Women with Gestational Diabetes. *Curr Diabetes Rev*. 2019;15(5):414-419. doi:10.2174/1573399814666181102100816
3. Breslavsky A, Frand J, Matas Z, Boaz M, Barnea Z, Shargorodsky M. Effect of high doses of vitamin D on arterial properties, adiponectin, leptin and glucose homeostasis in type 2 diabetic patients. Clin Nutr. 2013;32(6):970-975. doi:10.1016/j.clnu.2013.01.020
4. Szymczak-Pajor I, Śliwińska A. Analysis of Association between Vitamin D Deficiency and Insulin Resistance. *Nutrients*. 2019;11(4):794. doi:10.3390/nu11040794
5. Wan Nik WNFH, Zulkeflee HA, Ab Rahim SN, Tuan Ismail TS. Association of vitamin D and magnesium with insulin sensitivity and their influence on glycemic control. World J Diabetes. 2023;14(1):26-34. doi:10.4239/wjd.v14.i1.26
6. Chinedu AA, FasaNRade OA, Coker HA, Ohwovoriole AE. Relationship between vitamin D levels and glycaemic control in type 2 diabetes mellitus patients in Lagos, Nigeria. Journal of Diabetology. 2017 May 1;8(2):32-6.
7. Tucker LA. Serum, dietary, and supplemental vitamin D levels and insulin resistance in 6294 randomly selected, non-diabetic US adults. Nutrients. 2022 Apr 28;14(9):1844.
8. Obuchowska A, Gorczyca K, Standyło A, Obuchowska K, Kimber-Trojnar Ż, Wierzchowska-Opoka M, et al. Effects of probiotic supplementation during pregnancy on the future maternal risk of metabolic syndrome. International journal of molecular sciences. 2022 Jul 26;23(15):8253.
9. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. bmj. 2021 Mar 29;372.
10. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. *Syst Rev*. 2016;5(1):210.
11. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Rob 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019;366:l4898.
12. Gharekhani A, Najafipour F, Baradaran H, Tagharrobi P, Rezaee H. The Effect of Treating Vitamin D Deficiency or Insufficiency on Serum Adiponectin, Leptin and Insulin Resistance of Type 2 Diabetes Mellitus Patients: A Pilot Study. *Iran J Pharm Res*. 2020;19(3):86-94. doi:10.22037/ijpr.2020.112067.13512
13. Arif MA, Rasheed MK, Ismaeel AA. Association between vitamin D levels and insulin resistance in patients with type 2 diabetes mellitus. *Adv Life Sci*. 2024;11(2):419-424.

14. Adeleye JO, Emuze ME, Esan A, Bamidele OT. Serum vitamin D status and its relationship with insulin resistance amongst a cohort of Nigerian patients with type 2 diabetes mellitus. Journal of Diabetology. 2023 Oct;14(4):220-5.
15. Zhang J, Li Y, Lai D, Lu D, Lan Z, Kang J, et al. Vitamin D status is negatively related to insulin resistance and bone turnover in Chinese non-osteoporosis patients with type 2 diabetes: A retrospective cross-section research. Frontiers in Public Health. 2022 Feb 11;9:727132.
16. Sun X, Yan T, Li Z, Zhou S, Peng W, Cui W, et al. Effects of endurance exercise and vitamin D supplementation on insulin resistance and plasma lipidome in middle-aged adults with type 2 diabetes. *Nutrients*. 2023;15(13):3027.
17. Said J, Lagat D, Kimaina A, Oduor C. Beta cell function, insulin resistance and vitamin D status among type 2 diabetes patients in Western Kenya. Scientific Reports. 2021 Feb 18;11(1):4084.
18. Hashim ZR, Qasim QA, ALabbood MH. The association of serum calcium and vitamin D with insulin resistance and beta-cell dysfunction among people with type 2 diabetes. *Arch Razi Inst*. 2022;77(5):1593-1600.
19. Gao Y, Chen Z, Ma Z. Vitamin D is positively associated with bone mineral density muscle mass and negatively with insulin resistance in senile diabetes mellitus. *Dis Markers*. 2022;2022:9231408.
20. Al-Shami AS, Alzumor M, Aladhal A, Al-Saban A. Association between vitamin D level and insulin resistance among patients with type 2 diabetes mellitus in Sana'a City. *BMC Endocr Disord*. 2025;25(1):152.
21. Sun LJ, Lu JX, Li XY, Zheng TS, Zhan XR. Effects of vitamin D supplementation on glucose and lipid metabolism in patients with type 2 diabetes mellitus and risk factors for insulin resistance. *World J Diabetes*. 2023;14(10):1514-1523.
22. Alvina A, Immanuel S, Harbuwono DS, Suyatna FD, Harahap A, Prihartono J, et al. Effect of Three and Six Months of Vitamin D Supplementation on Glycemic Control and Insulin Resistance in Type 2 Diabetes Mellitus: Randomized Placebo-controlled Trial. *Indones Biomed J*. 2023;15(3):287-295.
23. Zhao H, Tang Y, Zheng C, Ren L, Song G. Vitamin D status is independently associated with insulin resistance in patients with type 2 diabetes mellitus. *Risk Manag Healthc Policy*. 2021;14:1393-1399.
24. Prasad BR, Imran T, Ahmed R, Me S, Kumar P. Influence of Serum Levels of Vitamin D on Insulin Resistance in Patients with Type II Diabetes Mellitus. *J Assoc Physicians India*. 2022;70(7):11-12.
25. Yin X, Chen JY, Huang XJ, Lai JH, Huang C, Yao W, et al. Association between vitamin D serum levels and insulin resistance assessed by HOMA-IR among non-diabetic adults in the United States: results from NHANES 2007–2014. *Front Nutr*. 2022;9:883904.
26. Ehrampoush E, Razzaz JM, Ghaemi A, Shahraki HR, Babaei AE, Osati S, et al. The association of vitamin D levels and insulin resistance. *Clin Nutr ESPEN*. 2021;42:325-332.
27. Wenclewska S, Szymczak-Pajor I, Drzewoski J, Bunk M, Śliwińska A. Vitamin D supplementation reduces both oxidative DNA damage and insulin resistance in the elderly with metabolic disorders. *Int J Mol Sci*. 2019;20(12):2891.
28. Khan MA, Fariduddin M, Alam MM. Vitamin D, Parathyroid Hormone and Insulin Resistance among Adults with Prediabetes: Vit. D, PTH and insulin prediabetes. *Bangladesh Med Res Counc Bull*. 2021;47(3):237-243.
29. Mirzaei-Azandaryani Z, Mohammad-Alizadeh-Charandabi S, Shaseb E, Abbasalizadeh S, Mirghafourvand M. Effects of vitamin D on insulin resistance and fasting blood glucose in pregnant women with insufficient or deficient vitamin D: a randomized, placebo-controlled trial. *BMC Endocr Disord*. 2022;22(1):254.
30. Schleu MF, Barreto-Duarte B, Arriaga MB, Araujo-Pereira M, Ladeia AM, Andrade BB, et al. Lower levels of vitamin D are associated with an increase in insulin resistance in obese Brazilian women. *Nutrients*. 2021;13(9):2979.
31. Safwan N, Mantzoros CS, Rahme M, Baddoura R, Halaby G, Fuleihan GE. Vitamin D supplementation at low (600 IU/day) or higher dose (3,750 IU/day) does not improve insulin resistance markers at one year: A randomized controlled trial. *Metab Open*. 2025;26:100357.
32. Tas E, Flint A, Libman I, Muzumdar R, Ou X, Williams DK, et al. The association between hepatic steatosis, vitamin D status, and insulin resistance in adolescents with obesity. *Obes Pillars*. 2025;14:100173.