Exploration of Endocrine and Metabolic Diseases

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Bidirectional relationship between vitamin D deficiency and type 1/type 2 diabetes mellitus: a systematic review and meta-analysis

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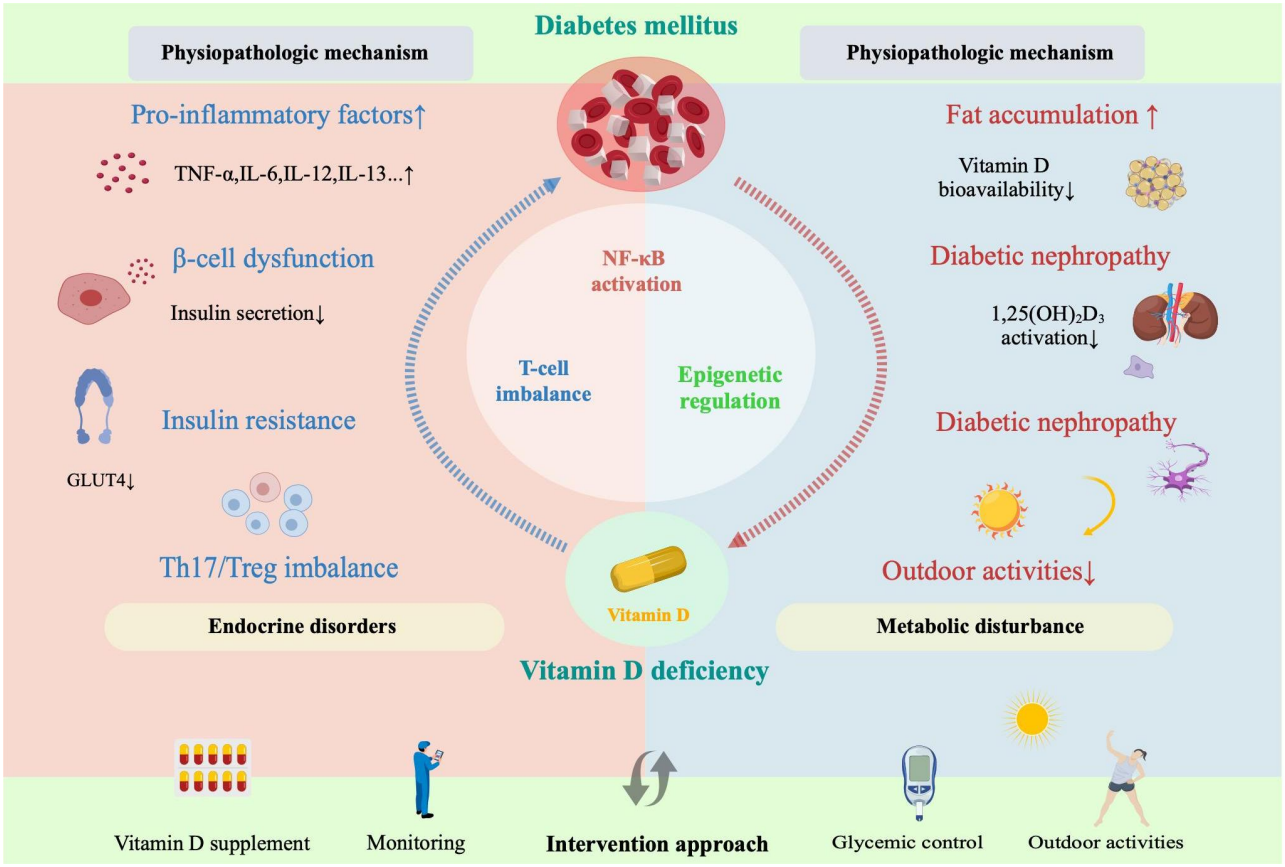
Abstract

Background: Diabetes mellitus and vitamin D deficiency (VDD) are widespread global health concerns with overlapping metabolic risks. Emerging evidence suggests a bidirectional relationship: VDD exacerbates insulin resistance, whereas diabetes mellitus disrupts vitamin D metabolism.

Methods: This meta-analysis was registered prospectively (PROSPERO CRD42025639951). We conducted a comprehensive search of PubMed, Embase, Web of Science, and the Cochrane Library from their inception to January 2025 for observational studies examining the bidirectional associations between VDD and diabetes mellitus. Studies were eligible if they (1) employed cohort or case-control designs, (2) defined VDD as serum 25-hydroxyvitamin D [25(OH)D] < 20 ng/mL, and (3) diagnosed diabetes mellitus according to the American Diabetes Association (ADA) criteria. Two reviewers independently extracted data and assessed study quality using the Newcastle-Ottawa scale. Pooled odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using random-effects models (STATA 15.1 and RevMan 5.4).

Results: Among 53 studies (n = 552,032), individuals with VDD had a 53% increased risk of developing type 2 diabetes mellitus (T2DM) (OR = 1.53, 95% CI: 1.38–1.70). Conversely, individuals with type 1 diabetes mellitus (T1DM) and T2DM had a 2.02-fold and 2.62-fold increased risk of VDD, respectively. Subgroup analyses demonstrated stronger associations in Asian populations (T1DM: OR = 2.21; Europe: OR = 1.65; P < 0.05 for regional difference) and among normal-weight T2DM patients (OR = 7.68, compared to obese: OR = 5.21).

Discussion: This meta-analysis reveals a bidirectional link between VDD and diabetes mellitus, emphasizing subtype- and phenotype-specific risk profiles. Clinically, routine monitoring of serum 25(OH)D levels is recommended for diabetic patients, particularly in high-risk subgroups such as individuals with T1DM or lean T2DM phenotypes, and suggests targeted vitamin D supplementation for high-risk groups. On a public health scale, fortifying staple foods with vitamin D in regions with high deficiency rates, such as Asia, could alleviate the dual burden of VDD and diabetes mellitus.



Graphical abstract. Vitamin D deficiency and diabetes: a bidirectional pathogenic interplay. ↑: increase/elevation; ↓: decrease/reduction. GLUT4: glucose transporter type 4; IL-6: interleukin 6; NF-κB: nuclear factor kappaB; Th17: T helper 17; TNF-α: tumor necrosis factor-alpha; Treg: regulatory T

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Keywords

Meta-analysis, vitamin D deficiency, prevalence, systematic review, diabetes

Introduction

Diabetes mellitus and vitamin D deficiency (VDD) represent significant global public health issues. Approximately 537 million adults have diabetes, with 90–95% diagnosed with type 2 diabetes mellitus (T2DM), and type 1 diabetes mellitus (T1DM) is rising by 3–5% annually [1]. The International Diabetes Federation projects that the global population aged 20–79 with diabetes will reach 700 million by 2045 [2]. Concurrently, about 1 billion people suffer from VDD, particularly prevalent in Asia and Africa due to limited sun exposure and dietary factors [3, 4]. Fu et al. [5] demonstrated that individuals with serum 25-hydroxyvitamin D [25(OH)D] levels ≥ 75 nmol/L had a multivariable-adjusted hazard ratio of 0.62 [95% confidence interval (CI): 0.56–0.70] for T2DM compared to those with levels < 25 nmol/L. Notably, within the sub-50 nmol/L range, increasing 25(OH)D concentration significantly reduces T2DM risk [5]. Khudayar et al. [6] demonstrated that 54.1% of patients with T2DM exhibited VDD, compared to 28.6% in the control group. This deficiency was significantly linked to the onset of T2DM ($P < 0.0001$) [6]. Vitamin D, a steroid hormone, plays a critical role in regulating bone mineral homeostasis and calcium metabolism. The predominant circulating form of vitamin D, 25(OH)D, determines an individual's vitamin D status [7]. In this study, VDD was defined as 25(OH)D levels below 20 ng/mL (50 nmol/L) as deficient, levels between 20–29 ng/mL as insufficient, and levels equal to or greater than 30 ng/mL as adequate, consistent with Endocrine Society Clinical Practice Guideline [8]. Experimental and observational evidence indicates that vitamin D signaling plays a role in insulin secretion and sensitivity, suggesting that VDD may elevate the

risk of diabetes [9]. Shared modifiable risk factors, such as obesity, physical inactivity, and advanced age, may confound the VDD-T1DM/T2DM relationship.

The available evidence suggests a bidirectional relationship between vitamin D and glucose homeostasis. Suboptimal vitamin D levels can impair pancreatic β-cell insulin secretion, a key process in regulating blood glucose. Additionally, VDD may diminish peripheral insulin sensitivity, thereby compromising glucose uptake by tissues, while chronic hyperglycemia and inflammation in diabetics can disrupt vitamin D metabolism [10]. Supporting this, Fu et al. [5] demonstrated a negative association between serum 25(OH)D levels and T2DM risk, even below the diabetes diagnostic threshold, and Nóvoa-Medina et al. [11] observed seasonal vitamin D variations and a higher deficiency prevalence in T1DM patients.

Prior meta-analyses were limited by their emphasis on one-way relationships. Dominguez et al. [12] focused solely on the impact of VDD on the onset of T2DM in older individuals, neglecting the occurrence of VDD in those already suffering from diabetes. Similarly, Yu et al. [13] exclusively investigated the effect of VDD on the development of T1DM across different populations, without taking into account the prevalence of VDD in individuals already diagnosed with diabetes. Recent clinical studies have expanded this understanding: Khudayar et al. [6] identified a 2.95-fold increased VDD risk in T2DM patients (95% CI: 2.28–3.80; $P < 0.0001$), while Chen et al. [14] found a 2.04-fold increased risk in the T1DM population (95% CI: 1.31–3.15; $P = 0.001$). This meta-analysis synthesizes data from 53 studies ($n = 552,032$) to systematically evaluate the bidirectional association between VDD and diabetes mellitus, stratified by subtypes (T1DM vs. T2DM) and phenotypic subgroups.

Materials and methods

Literature searches

The meta-analysis was registered in PROSPERO (CRD42025639951). Comprehensive searches were conducted in PubMed, Embase, Web of Science, and the Cochrane Library for articles published from database inception to January 2025. The search strategy employed keywords such as VDD, diabetes mellitus, type 1 diabetes mellitus, type 2 diabetes mellitus, T1DM, and T2DM. Table S1 details the search strategy. This study aimed to: (1) assess the prevalence of diabetes mellitus in individuals with VDD and vice versa in those with T1DM/T2DM; (2) compare diabetes mellitus prevalence in VDD patients with non-VDD controls; and (3) compare VDD prevalence in T1DM/T2DM patients with non-diabetic controls.

Study selection

Articles were selected based on the following criteria: (1) cohort or case-control studies (there were no limits on sample size when including case-control studies); (2) reporting the bidirectional prevalence of VDD (< 20 ng/mL or 50 nmol/L) [8] versus diabetes mellitus (T1DM/T2DM), and diagnosed diabetes mellitus according to the American Diabetes Association (ADA) criteria [15]; (3) evaluating the clinical characteristics of patients with VDD and diabetes mellitus, providing detailed data for analysis. Studies were excluded if they: (1) lacked data convertible to vitamin D < 20 ng/mL (e.g., only reported ≥ 30 ng/mL subgroup); (2) involved pre-diabetic populations (impaired fasting glycemia, glucose intolerance, and/or glycated hemoglobin A1c 5.7–6.4% or 39–47 mmol/mol) [15] or gestational diabetes; (3) involved duplicate populations; (4) were conference abstracts, letters, reviews, animal studies, cellular experiments, non-English papers, or unavailable data; (5) lacked access to the full publication. Two researchers (HH and SS) independently screened titles, abstracts, and full texts for eligibility, and a third investigator (DL) independently decided on the inclusion of any relevant articles cited within the retrieved articles.

Data extraction and quality assessment

Two authors (HH and SS) independently reviewed the full-text articles and extracted data on (1) authorship, (2) publication year, (3) country or region, (4) study design, (5) diagnostic criteria for VDD and diabetes mellitus, (6) population, and (7) baseline characteristics. Key variables included (1) total

participants, (2) participants with T1DM/T2DM, (3) participants with VDD, and (4) mean and standard deviation of clinical characteristics. Discrepancies in data extraction, such as differing interpretations of outcome definitions, were resolved through consensus discussions, with unresolved issues adjudicated by a third investigator (DL). Data were recorded on standardized forms and verified by two investigators (HH and SS). Study quality was evaluated using the Newcastle-Ottawa scale [16], assessing selection, exposure/outcome, and comparability; a score of 7–9 denotes high quality. Using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework, we evaluated the evidence for each outcome, categorizing it as "high", "moderate", "low", or "very low" quality [17].

Data synthesis

The combined prevalence and 95% CIs of diabetes mellitus and VDD were analyzed using generalized inverse variance statistics [18]. This method addresses between-study heterogeneity by inversely weighting individual study estimates to their variance, making it ideal for meta-analyses with diverse sample sizes and measurement scales, enabling robust pooling under a random-effects model. Mantel-Haenszel statistics calculated odds ratios (ORs) and 95% CIs to compare diabetes mellitus prevalence in VDD patients versus non-VDD controls, VDD prevalence in T1DM patients versus non-T1DM controls, and VDD prevalence in T2DM patients versus non-T2DM controls. Data were pooled using a random effects model. Heterogeneity was assessed with the Higgins I^2 statistic, where $I^2 > 50\%$ indicated significant heterogeneity. Sensitivity analyses involved removing each study individually to re-estimate effect sizes. Publication bias was evaluated using funnel plots and Egger et al. [19] test, with $P \leq 0.05$ indicating statistical significance. If significant bias was detected, Duval and Tweedie [20] trim and fill method was applied for adjustment. Subgroup analyses considered region, study design, follow-up duration, sample size, mean/median age, mean/median body mass index (BMI), assay method, and latitude climate zone. Analyses were conducted using RevMan 5.4 [Review Manager (RevMan) Version 5.4, The Cochrane Collaboration, 2020] and STATA 15.1 (StataCorp Stata MP 15.1, United States).

Results

Characteristics of included studies and quality assessment

Fifty-three studies met the inclusion criteria. Of these, five examined the prevalence of T2DM in patients with VDD [5, 21–24], 27 assessed VDD prevalence in patients with T2DM [6, 25–50], 23 focused on VDD in T1DM patients [11, 14, 30, 40, 51–69], and two examined VDD prevalence in patients with both T1DM and T2DM [30, 40], with data extracted separately. Clinical characteristics were extracted from all studies. Ten studies were conducted in Western countries, six in African countries, and 37 in Asia. Figure 1 presents the article screening flowchart [70], while Table 1 details the basic characteristics. All studies were observational, comprising six cohort studies and 47 case-control studies. Among them, 23 were high-quality studies with scores ranging from 7 to 9, and 30 had a score of 6 (see Tables S2 and S3). The assessment revealed that most of the 51 outcomes were of low or very low quality. Specifically, two outcomes (3.9%) were rated as moderate quality, 19 outcomes (37.25%) as low quality, and 30 outcomes (58.8%) as very low quality (see Table S4).

Prevalence of T2DM in patients with VDD

Five prospective cohort studies examined T2DM prevalence in patients with VDD. Among VDD patients (n = 537,019), T2DM prevalence was significantly higher compared to non-VDD controls [OR: 1.53, 95% CI: 1.38–1.70, 95% prediction interval (PI): 1.16–2.02, I^2 = 66%, $P < 0.00001$; very low (the quality of evidence is expressed as "GRADE"); Figure 2]. Sensitivity analyses identified a source of heterogeneity (Figure S1): one study (Veronese et al. [24]) focused on community-dwelling older adults aged 65 and above. Excluding this study, the combined OR for T2DM in VDD patients was 1.65 (95% CI: 1.59–1.70, I^2 = 0%, $P < 0.00001$). Subgroup analysis (Table 2) showed a combined OR of 1.66 (95% CI: 1.60–1.71, I^2 = 0%, $P < 0.00001$; low) for VDD patients with follow-up ≥ 5 years, and 1.34 (95% CI: 0.95–1.88, I^2 = 84%, P = 0.09; very low) for those with follow-up < 5 years. The articles were categorized into two groups based on sample size (n ≥

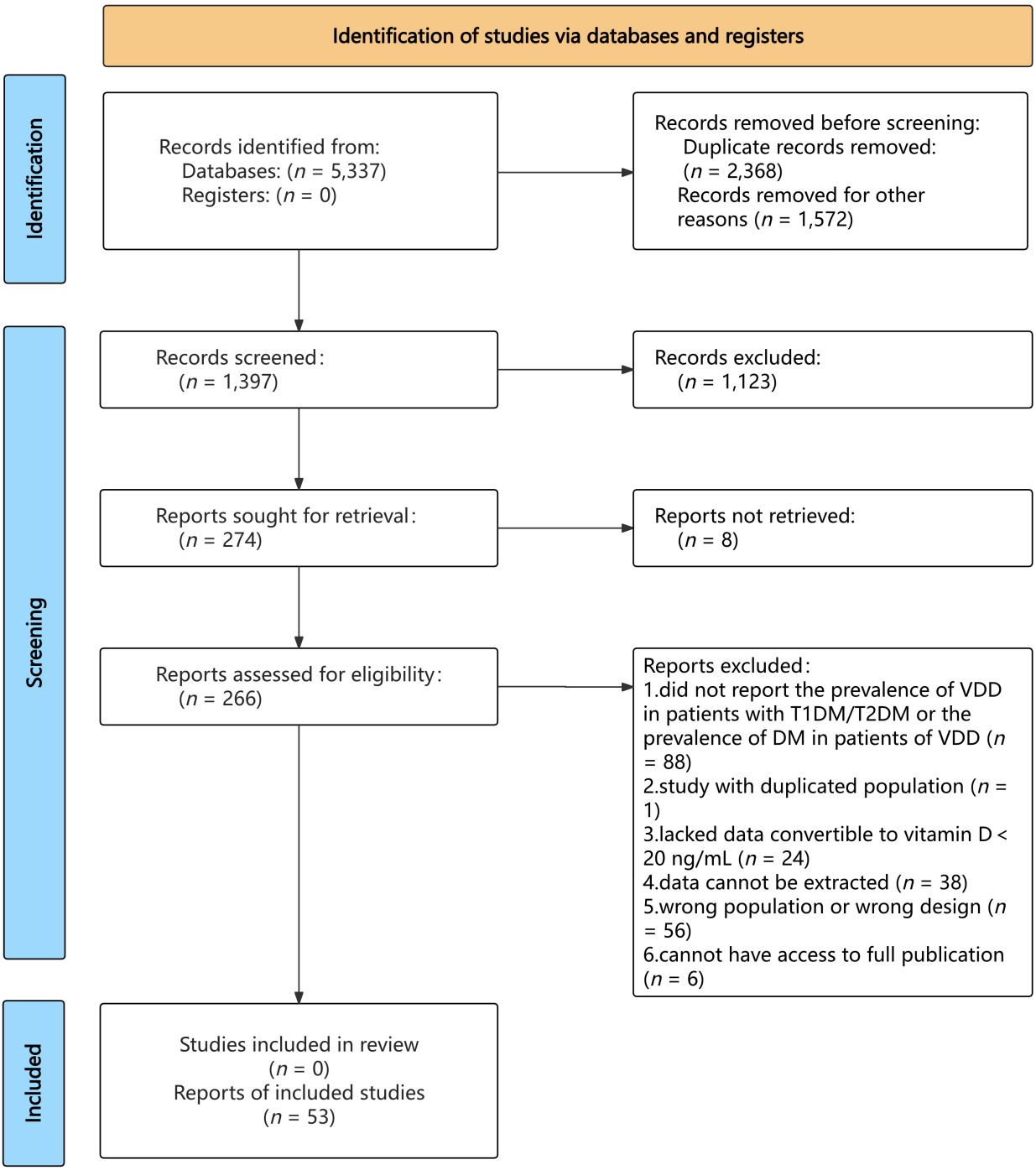

Figure 1. Flowchart of the selection of studies. DM: diabetes mellitus; T1DM: type 1 diabetes mellitus; T2DM: type 2 diabetes mellitus; VDD: vitamin D deficiency

Note. Adapted from [70]. CC BY

1,000 and $n < 1,000$). For patients with VDD and sample sizes ≥ 1,000, the combined OR for T2DM was 1.54 (95% CI: 1.38–1.71, $I^2 = 73\%$, $P < 0.00001$; low). For sample sizes < 1,000, the combined OR was 1.24 (95% CI: 0.65–2.38, $P = 0.51$; very low). Three studies employing the chemiluminescence immunoassay (CLIA) test method were categorized, revealing a combined OR of 1.65 (95% CI: 1.60–1.70, $I^2 = 0\%$, $P < 0.00001$; low) for diabetes. Subgroup analyses revealed no significant OR for T2DM in VDD patients across age, BMI, sample size < 1,000, and follow-up < 5 years compared to the non-VDD population, likely due to the limited number of studies. Egger's test ($P = 0.109$) indicated no publication bias, and the funnel plot was symmetric.

Table 1. The baseline characteristics of the included studies

Authors	Year	Study period	Country	Study design	Population	Number of patients		Follow-up (median/mean)	Mean/median age		Male (*n*)		BMI (kg/m^2)	
						On camp	Off camp		On camp	Off camp	On camp	Off camp	On camp	Off camp
Nóvoa-Medina et al. [11]	2023	2016–2022	Spain	Retrospective	T1DM patients age < 15 years	146	346	NA	8.4 ± 3.9	10 ± 2.7	83	149	17.3 ± 4.5	17.6 ± 6.1
Boyraz et al. [29]	2016	2013.10.1–2014.4.30	Turkey	Retrospective	Patients with T2DM	126	62	NA	58.90 ± 9.436	48.016 ± 9.32	NA	NA	28.60 ± 3.71	26.764 ± 4.317
Khudayar et al. [6]	2022	2020.10–2021.9	Pakistan	Retrospective	Patients with T2DM aged 30 to 60 years	525	525	NA	50 ± 5.5	52.1 ± 5.7	284	280	NA	NA
Alqudsi et al. [52]	2019	2017.5–2017.9	Saudi Arabia	Retrospective	Teenagers with T1DM aged 12 to 18 years	49	49	NA	14.52 ± 2.06	13.92 ± 2.03	24	24	NA	NA
Parveen et al. [42]	2019	NA	India	Retrospective	Patients with T2DM aged between 19 and 65 years	44	44	NA	45.7	44.91	23	26	26.1	25.33
Razip et al. [43]	2021	2021.5.21–2021.7.1	Malaysia	Retrospective	Patients with T2DM aged 30 to 65 years	50	50	NA	NA	NA	26	28	28.7 ± 4.80	27.3 ± 4.63
Tsur et al. [23]	2013	2008.7–2012.6	Israel	Prospective	People aged 40 to 70 years	62,226	55,734	2 years	NA	NA	NA	NA	NA	NA
Ma et al. [41]	2020	2015.3–2019.5	China	Retrospective	Patients with T2DM	674	521	NA	62.92 ± 2.0	62.4 ± 3.3	319	246	NA	NA
Thrailkill et al. [66]	2011	NA	USA	Retrospective	Patients with T1DM aged 14 to 40 years	115	55	NA	20.86	24.3	54	24	25.04	25.2
Kumar et al. [25]	2017	NA	India	Retrospective	Patients with T2DM aged 30 to 70 years	78	69	NA	48.50	44	33	33	NA	NA
Yadavelli et al. [68]	2023	2021.1–2022.5	India	Retrospective	Children with T1DM aged 6 to 15 years	50	50	NA	11.36	NA	21	38	NA	NA
Lari et al. [39]	2022	2013–2017	Kuwait	Retrospective	Patients with T2DM	203	162	NA	57.3	29.26	60	51	33.57	29.03
Daga et al. [30]	2012a	NA	India	Retrospective	Newly diagnosed young patients with T1DM (under 25 years old)	13	41	NA	15.15	16.98	6	NA	16.81	17.47
Daga et al. [30]	2012b	NA	India	Retrospective	Young patients with newly diagnosed diabetes (under 25 years old)	58	41	NA	16.93	16.98	26	NA	17.23	17.47

Table 1. The baseline characteristics of the included studies (*continued*)

Authors	Year	Study period	Country	Study design	Population	Number of patients		Follow-up (median/mean)	Mean/median age		Male (*n*)		BMI (kg/m^2)	
						On camp	Off camp		On camp	Off camp	On camp	Off camp	On camp	Off camp
Salih et al. [47]	2021	2018.2.1–2018.7.30	Iraq	Retrospective	Patients with T2DM who are over 25 years old	155	155	NA	49.94	48.95	68	70	NA	NA
Tang et al. [49]	2023	2019.1–2021.1	China	Retrospective	Patients with T2DM, with or without foot ulcers	256	100	NA	55.3	55.1	142	57	NA	NA
Bae et al. [54]	2018	2011	South Korea	Retrospective	Children and adolescents aged 6 to 20 years diagnosed with T1DM	85	518	NA	14.5 ± 4.4	13.8 ± 3.8	37	239	NA	NA
Borkar et al. [56]	2010	2007.7–2008.12	India	Retrospective	Children aged 6 to 12 years who are newly diagnosed with T1DM	50	50	NA	8.63 ± 2.01	8.48 ± 1.58	29	35	15.74 ± 1.88	16.25 ± 2.43
Devaraj et al. [57]	2011	NA	USA	Retrospective	T1DM patients aged 18 years or older	50	36	NA	33.5 ± 11.1	31 ± 11	17	14	25.5 ± 5.5	25 ± 5
Rodrigues et al. [45]	2019	2012.6–2013.9	Brazil	Retrospective	T2DM patients aged 32 to 70 years	101	62	NA	56 ± 13	53 ± 18	19	12	NA	NA
Reddy et al. [44]	2015	2010.10–2013.3	India	Retrospective	Patients with T2DM	164	99	NA	NA	NA	94	54	NA	NA
Durgarao et al. [32]	2017	2016.12–2017.1	India	Retrospective	T2DM patient aged 40 to 60 years	100	100	NA	49.76 ± 5.21	48.52 ± 6.03	63	66	NA	NA
Jayashri et al. [38]	2020	2012–2013	India	Prospective	Diabetes patients aged between 20 and 80 years	300	900	10 years	NA	NA	NA	NA	NA	NA
Sarma et al. [48]	2018	2015.8–2016.12	India	Retrospective	Patients with T2DM	40	20	NA	49.65 ± 9.78	48.45 ± 8.73	NA	NA	24.51 ± 3.19	22.26 ± 1.32
Lin et al. [40]	2019a	NA	China	Retrospective	Patients with T1DM	56	42	NA	19.32 ± 4.59	20.79 ± 3.29	23	17	NA	NA
Lin et al. [40]	2019b	NA	China	Retrospective	Patients with T2DM	41	28	NA	60.71 ± 16.26	54.07 ± 11.04	23	11	NA	NA
Veronese et al. [24]	2014	1995–2009	Italy	Prospective	Community-dwelling elderly people aged 65 and older without diabetes	725	1,502	4.4 years	79.05	74.6	174	748	27.14	27.17

Table 1. The baseline characteristics of the included studies (*continued*)

Authors	Year	Study period	Country	Study design	Population	Number of patients		Follow-up (median/mean)	Mean/median age		Male (*n*)		BMI (kg/m^2)	
						On camp	Off camp		On camp	Off camp	On camp	Off camp	On camp	Off camp
Hassan et al. [36]	2024	2022.3–2022.5	Sudan	Retrospective	Patients with T2DM from Sudan who are 18 years old or older	88	88	NA	55	55	40	42	27	26
Husemoen et al. [21]	2012	1993–2010.12.31	Denmark	Prospective	Men and women aged 41 to 71 years	11,423	25,430	16.4 years	NA	NA	NA	NA	NA	NA
Liu et al. [61]	2018	NA	China	Retrospective	Children and adolescents with T1DM	296	295	NA	8.66	8.4	147	148	NA	NA
Greer et al. [60]	2013	2007.3–2008.3	Australia	Retrospective	Children with T1DM	56	56	NA	11.55	8.67	28	30	NA	NA
Bayani et al. [28]	2014	2011.10–2012.9	Iran	Retrospective	People aged 30 to 60 years with T2DM	120	120	NA	51.2 ± 7.98	50.6 ± 7.73	50	50	NA	NA
Wang et al. [50]	2018	2013.6–2013.7	China	Retrospective	Patients with T2DM	397	397	NA	NA	NA	NA	NA	26.34 ± 3.61	25.45 ± 3.58
Saleem et al. [46]	2017	2017.1.1–2017.8.31	Pakistan	Retrospective	Patients with T2DM	100	100	NA	48.55 ± 14.62	46.15 ± 12.43	53	51	NA	NA
Majeed et al. [62]	2023	2013.3–2017.4	United Arab Emirates	Retrospective	Children and adolescents aged 4 to 19 years with T1DM	148	296	NA	12.5	11.9	66	123	NA	NA
Esteghamati et al. [33]	2015	2012.3–2013.8	Iran	Retrospective	Adults or adolescents aged 15 years and above with T2DM	1,195	209	NA	55.8 ± 10.4	52.5 ± 11.1	555	97	29.7 ± 5.2	28.5 ± 4.8
Alduraywish et al. [26]	2019	2016.11.1–2017.4.19	Saudi Arabia	Retrospective	Patients with T2DM	290	126	NA	44.45 ± 16.96	47.82 ± 13.29	NA	NA	27.66 ± 4.998	29.07 ± 4.595
Rochmah et al. [65]	2022	2019.3–2019.5	Indonesia	Retrospective	Children with T1DM under the age of 18	31	24	NA	11.22 ± 4.15	7.55 ± 3.18	18	10	17.35 ± 4.32	18.54 ± 5.23
Nam et al. [64]	2019	NA	South Korea	Retrospective	Patients with T1DM under the age of 20	96	156	NA	14.7 ± 4.3	14.0 ± 4.2	42	67	0.2 ± 0.1	–0.1 ± 0.1
Bajaj et al. [27]	2014	NA	India	Retrospective	Patients with T2DM aged 8 to 70 years	158	130	NA	52.85 ± 8.26	51.87 ± 6.43	95	80	NA	NA
Chen et al. [14]	2022	2017–2019	China	Retrospective	Children with T1DM	141	200	NA	6.3 ± 3.3	5.6 ± 3.6	59	114	NA	NA

Table 1. The baseline characteristics of the included studies (*continued*)

Authors	Year	Study period	Country	Study design	Population	Number of patients		Follow-up (median/mean)	Mean/median age		Male (*n*)		BMI (kg/m^2)	
						On camp	Off camp		On camp	Off camp	On camp	Off camp	On camp	Off camp
Bin-Abbas et al. [55]	2011	2010.6–2010.9	Saudi Arabia	Retrospective	Saudi children diagnosed with T1DM for more than 5 months	100	100	NA	9.5 ± 3.2	8.9 ± 2.1	41	48	17.6 ± 3.6	17.9 ± 3.0
Gendy et al. [35]	2018	2016.12–2017.11	Egypt	Retrospective	Patients with T2DM	50	50	NA	52.48 ± 6.55	51 ± 8.2	10	16	33.03 ± 6.07	30.57 ± 7.68
Ahmed et al. [58]	2019	2017.12–2018.11	Egypt	Retrospective	Children with T1DM (before vitamin D treatment)	50	50	NA	11.16 ± 3.27	10.97 ± 2.77	24	25	17.50 ± 3.24	17.32 ± 2.92
Fondjo et al. [34]	2017	2015.10–2015.12	Ghana	Retrospective	Patients with T2DM	118	98	NA	58.81 ± 0.90	57.79 ± 1.49	25	22	26.05 ± 0.47	23.73 ± 0.51
Mihçioğlu and Hatun [63]	2022	2009.3.1–2010.9.1	Turkey	Retrospective	Patients newly diagnosed with T1DM	80	30	NA	8.38 ± 4.25	8.45 ± 5.39	44	15	16.08 ± 2.90	18.72 ± 5.68
Ghandchi et al. [59]	2012	2008–2009	Iran	Retrospective	Patients with T1DM aged 5 to 25 years	60	120	NA	14.4	15.15	32	52	21.4	21
Abd-Allah et al. [51]	2014	NA	Egypt	Retrospective	Patients with T1DM	120	120	NA	11.7 ± 2.8	11.1 ± 2.6	42	48	18.5 ± 4.3	21.6 ± 1.5
Ziaei-Kajbaf et al. [69]	2018	2015.10–2016.3	Iran	Retrospective	Children and teenagers aged 1 to 15 years	85	85	NA	8.73 ± 4.05	7.62 ± 3.68	40	44	16.52	15.92
Azab et al. [53]	2013	2012.1–2012.12	Egypt	Retrospective	Children and adolescents aged 6 to 16 years with T1DM	80	40	NA	11.4 ± 2.5	10.8 ± 2.3	34	24	23.6 ± 5.7	21.8 ± 4.7
Wierzbicka et al. [67]	2016	NA	Poland	Retrospective	Teenage patients with T1DM	60	40	NA	15.1 ± 1.9	15.6 ± 1.8	28	20	21.1 ± 3.1	21.7 ± 2.9
Pilz et al. [22]	2012	2000–2009	Netherlands	Prospective	People aged 50 to 75 years	106	174	7.5 ± 0.5 years	NA	NA	NA	NA	NA	NA
Fu et al. [5]	2024	2006–2023.3.30	UK	Prospective	Adults aged 40 to 69 years	205,609	174,090	14.1 years	55.53	57	111,440	94,487	27.62	26.4
Dhas et al. [31]	2019	2016.3–2018.2	India	Retrospective	Adults with T2DM aged 30 to 50 years	90	90	-	41.83 ± 5.91	37.97 ± 6.14	50	52	28.46 ± 3.68	25.59 ± 3.95
Iqbal et al. [37]	2017	2013.1–2015.7	Pakistan	Retrospective	Adult patients with T2DM	165	165	-	48.82	46.27	116	116	28.96	25.24

BMI: body mass index; NA: not available; T1DM: type 1 diabetes mellitus; T2DM: type 2 diabetes mellitus; UK: United Kingdom; USA: United States of America

Table 2. Subgroup analyses

Subgroup	Effects of VDD on the risk of T2DM						Effects of T1DM on the risk of VDD						Effects of T2DM on the risk of VDD					
	Study	OR (95% CI)	*P* value	I^2	Egger's test	GRADE	Study	OR (95% CI)	*P* value	I^2	Egger's test	GRADE	Study	OR (95% CI)	*P* value	I^2	Egger's test	GRADE
Total	5	1.53 [1.38–1.70]	< 0.00001	66%	0.109	Very low	23	2.02 [1.42–2.89]	0.0001	81%	0.055	Low	27	2.62 [1.85–3.70]	< 0.00001	90%	0.038	Low
Study design																		
Prospective	5	1.53 [1.38–1.70]	< 0.00001	66%	0.109	Very low	NA	NA	NA	NA	NA	NA	1	1.64 [1.25–2.14]	0.0003	NA	NA	Very low
Retrospective	NA	NA	NA	NA	NA	NA	23	2.02 [1.42–2.89]	0.0001	81%	0.055	Low	26	2.71 [1.86–3.95]	< 0.00001	90%	0.038	Low
Follow-up																		
≥ 5 years	3	1.66 [1.60–1.71]	< 0.00001	0%	NA	Low	NA	NA	NA	NA	NA	NA	1	1.64 [1.25–2.14]	0.0003	NA	NA	Very low
< 5 years	2	1.34 [0.95–1.88]	0.09	84%	NA	Very low	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Region																		
Asia	1	1.56 [1.43–1.70]	< 0.00001	NA	NA	Very low	15	2.21 [1.55–3.15]	< 0.0001	74%	0.165	Low	23	2.38 [1.67–3.39]	< 0.00001	90%	0.049	Low
Europe	4	1.45 [1.17–1.78]	0.0005	71%	NA	Very low	2	1.65 [1.03–2.64]	0.04	0%	NA	Very low	NA	NA	NA	NA	NA	NA
North America	NA	NA	NA	NA	NA	NA	2	1.67 [0.83–3.37]	0.15	0%	NA	Very low	NA	NA	NA	NA	NA	NA
Africa	NA	NA	NA	NA	NA	NA	3	3.71 [0.26–53.46]	0.33	96%	NA	Very low	3	4.75 [0.55–41.06]	0.16	92%	NA	Very low
Australia	NA	NA	NA	NA	NA	NA	1	1.73 [0.39–7.62]	0.47	NA	NA	Very low	NA	NA	NA	NA	NA	NA
South America	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	1	11.50 [4.76–27.75]	< 0.00001	NA	NA	Low
Sample size																		
≥ 1,000	4	1.54 [1.38–1.71]	< 0.00001	73%	NA	Low	NA	NA	NA	NA	NA	NA	4	2.44 [1.74–3.42]	< 0.00001	79%	NA	Low
< 1,000	1	1.24 [0.65–2.38]	0.51	NA	NA	Very low	23	2.02 [1.42–2.89]	0.0001	81%	0.055	Low	23	2.80 [1.73–4.53]	< 0.0001	91%	0.024	Low
Mean/median age																		
≥ 50 years	2	1.38 [0.92–2.06]	0.12	90%	NA	Very low	NA	NA	NA	NA	NA	NA	12	3.29 [2.02–5.34]	< 0.00001	86%	0.111	Low
< 50 years	NA	NA	NA	NA	NA	NA	23	2.02 [1.42–2.89]	0.0001	81%	0.055	Low	11	2.87 [1.53–5.37]	0.001	90%	0.014	Very low

Table 2. Subgroup analyses (*continued*)

Subgroup	Effects of VDD on the risk of T2DM						Effects of T1DM on the risk of VDD						Effects of T2DM on the risk of VDD					
	Study	OR (95% CI)	*P* value	I^2	Egger's test	GRADE	Study	OR (95% CI)	*P* value	I^2	Egger's test	GRADE	Study	OR (95% CI)	*P* value	I^2	Egger's test	GRADE
Mean/median BMI																		
≥ 30 kg/m^2	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	2	5.21 [0.08–332.64]	0.44	88%	NA	Very low
≥ 25, < 30 kg/m^2	2	1.38 [0.92–2.06]	0.12	90%	NA	Very low	2	1.67 [0.83–3.37]	0.15	0%	NA	Very low	9	1.30 [0.71–2.37]	0.4	92%	NA	Very low
≥ 18.5, < 25 kg/m^2	NA	NA	NA	NA	NA	NA	4	1.23 [0.32–4.63]	0.76	90%	NA	Very low	2	7.68 [3.94–14.95]	< 0.00001	0%	NA	Moderate
< 18.5 kg/m^2	NA	NA	NA	NA	NA	NA	9	2.91 [1.71–4.94]	< 0.0001	67%	NA	Low	1	40.38 [5.08–320.74]	0.0005	NA	NA	Low
Assay method																		
CLIA	3	1.65 [1.60–1.70]	< 0.00001	0%	NA	Low	7	1.98 [1.02–3.83]	0.04	80%	NA	Very low	3	1.83 [0.86–3.90]	0.12	74%	NA	Very low
RIA	2	1.12 [0.88–1.42]	0.37	0%	NA	Very low	3	2.61 [1.86–3.68]	< 0.00001	0%	NA	Moderate	2	7.79 [0.43–141.44]	0.16	87%	NA	Very low
ELISA	NA	NA	NA	NA	NA	NA	6	2.18 [0.72–6.55]	0.17	92%	NA	Very low	12	2.64 [1.50–4.64]	0.0008	90%	0.004	Low
HPLC	NA	NA	NA	NA	NA	NA	4	1.94 [0.87–4.34]	0.11	63%	NA	Very low	4	2.91 [1.38–6.11]	0.005	77%	NA	Very low
LC-MS/MS	NA	NA	NA	NA	NA	NA	1	2.04 [1.31–3.15]	0.001	NA	NA	Very low	NA	NA	NA	NA	NA	NA
Latitude climate zone																		
Temperate zone	5	1.53 [1.38–1.70]	< 0.00001	66%	0.109	Very low	19	1.94 [1.35–2.80]	0.0004	81%	0.055	Very low	17	2.54 [1.59–4.05]	< 0.0001	92%	0.038	Low
Tropical zone	NA	NA	NA	NA	NA	NA	4	2.55 [0.56–11.61]	0.23	83%	NA	Very low	10	2.89 [1.69–4.94]	0.0001	83%	0.147	Low

BMI: body mass index; CI: confidence interval; CLIA: chemiluminescence immunoassay; ELISA: enzyme-linked immunosorbent assay; GRADE: Grading of Recommendations, Assessment, Development, and Evaluation; HPLC: high performance liquid chromatography; LC-MS/MS: Liquid chromatography-tandem mass spectrometry; NA: not available; ORs: odds ratios; RIA: radioimmunoassay; T1DM: type 1 diabetes mellitus; T2DM: type 2 diabetes mellitus; VDD: vitamin D deficiency

Prevalence of VDD in people with T1DM

Twenty-three case-control studies were included to assess the prevalence of VDD in individuals with T1DM. The overall analysis, involving 4,816 T1DM patients, revealed a significantly higher prevalence of VDD in comparison to non-T1DM controls (OR: 2.02, 95% CI: 1.42–2.89, 95% PI: 0.43–9.50, I^2 = 81%, P = 0.0001; low; Figure 3). Sensitivity analyses, excluding six specific studies [51, 58, 62, 63, 68, 69], demonstrated that the combined OR for VDD in T1DM patients was 2.19 (95% CI: 1.86–2.58, I^2 = 0%, P < 0.00001), indicating a potential source of heterogeneity (Figure S2). There was substantial heterogeneity among the studies (I^2 = 81%,

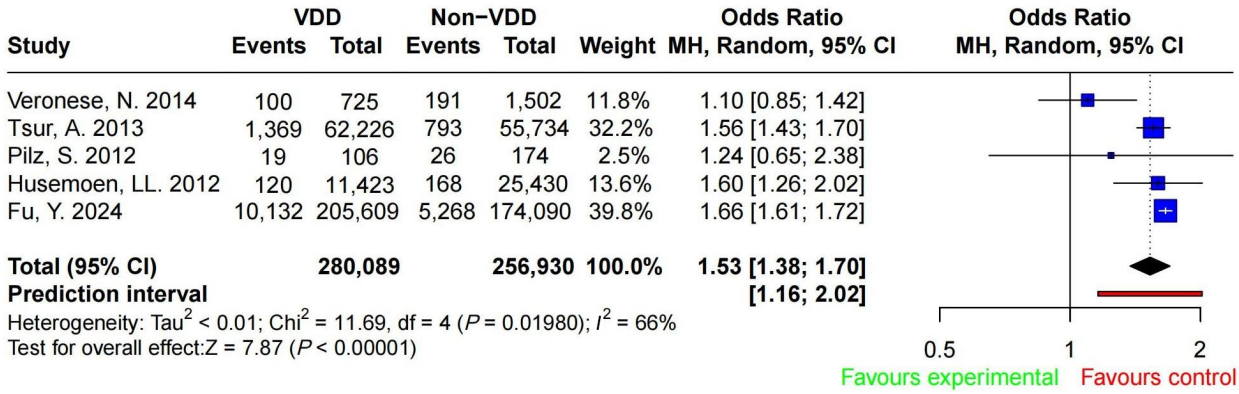

Figure 2. Comparison of the prevalence of T2DM in patients with and without VDD. CI: confidence interval; MH: Mantel-Haenszel; T2DM: type 2 diabetes mellitus; VDD: vitamin D deficiency

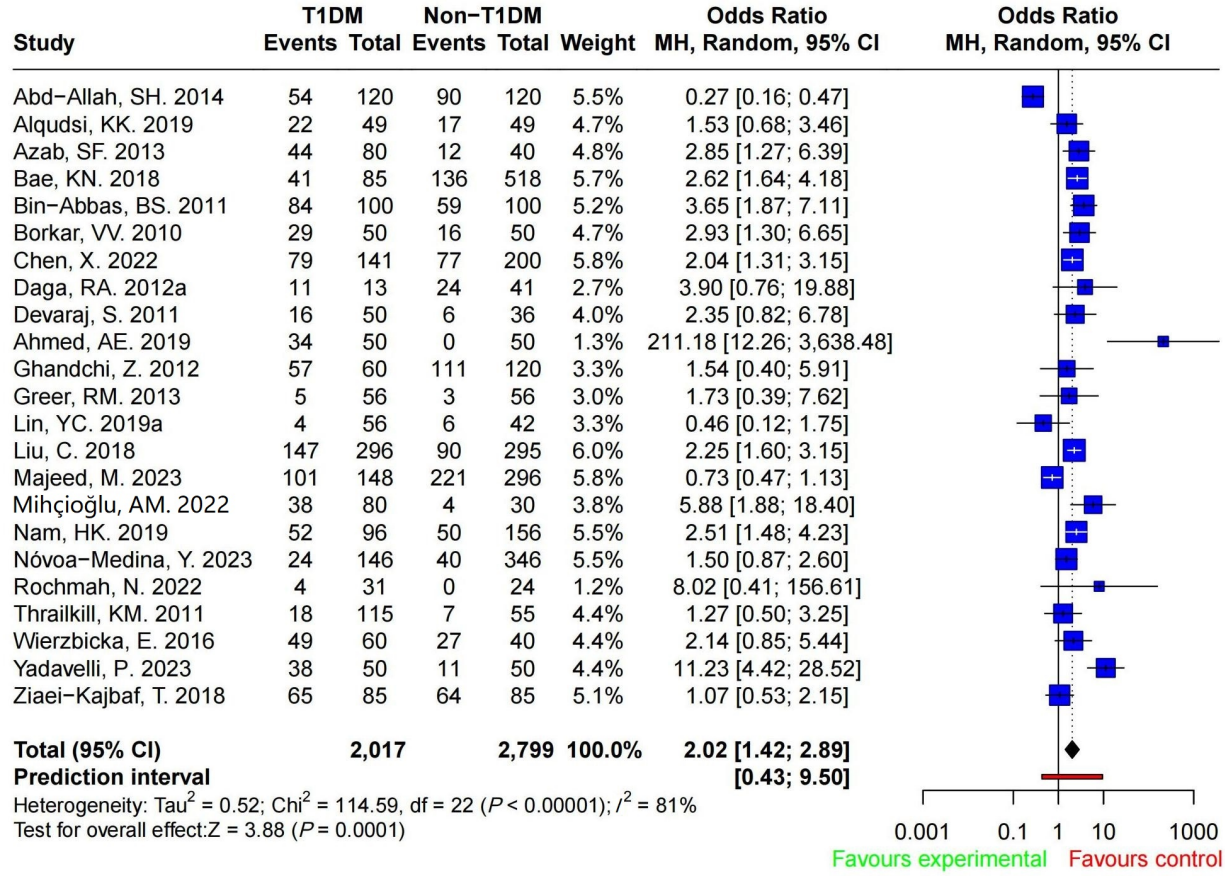

Figure 3. Comparison of the prevalence of VDD in patients with and without T1DM. CI: confidence interval; MH: Mantel-Haenszel; T1DM: type 1 diabetes mellitus; VDD: vitamin D deficiency

95% PI: 0.43–9.50). This variation could potentially be explained by differences in population characteristics (e.g., age, geographic latitude) and inconsistencies in the detection methodologies. Subgroup analyses (Table 2) indicated a significantly elevated risk of VDD in Asian and European populations with T1DM compared to non-T1DM controls, with combined ORs of 2.21 (95% CI: 1.55–3.15, I^2 = 74%, P < 0.0001; low) and 1.65 (95% CI: 1.03–2.64, I^2 = 0%, P = 0.04; very low), respectively. Subgroup analysis revealed that among the studies utilizing the radioimmunoassay (RIA) method for detection, three studies reported a combined OR for diabetes of 2.61 (95% CI: 1.86–3.68, I^2 = 0%, P < 0.00001; moderate). In contrast, among the studies employing the CLIA method, seven studies indicated a combined OR for diabetes of 1.98 (95% CI: 1.02–3.83, I^2 = 80%, P = 0.04; very low). Nineteen studies conducted in temperate regions showed a combined OR of 1.94 (95% CI: 1.35–2.80, I^2 = 81%, P = 0.0004; very low) for VDD in patients with T1DM. Assessment using the Egger test (P = 0.055) revealed no publication bias, and funnel plots exhibited symmetry.

Prevalence of VDD in people with T2DM

A prospective cohort study and 26 case-control studies examined the prevalence of VDD in patients with T2DM. Among T2DM patients (n = 10,197), VDD prevalence was significantly higher compared to non-T2DM controls (OR: 2.62, 95% CI: 1.85–3.70, 95% PI: 0.48–14.33, I^2 = 90%, P < 0.00001; low; Figure 4). Sensitivity analyses confirmed stable results after excluding one study (Figure S3). Subgroup analysis (Table 2) of the 26 case-control studies yielded a combined OR of 2.71 (95% CI: 1.86–3.95, I^2 = 90%, P < 0.00001; low) for VDD in the T2DM group. Studies were categorized by sample size (n ≥ 1,000 and n < 1,000). For sample sizes ≥ 1,000, the combined OR was 2.44 (95% CI: 1.74–3.42, I^2 = 79%, P < 0.00001; low), while for sizes < 1,000, it was 2.80 (95% CI: 1.73–4.53, I^2 = 91%, P < 0.0001; low). In temperate regions, VDD patients with T2DM exhibited a combined OR of 2.54 (95% CI: 1.59–4.05, I^2 = 92%, P < 0.0001; low), whereas in tropical regions, the combined OR was 2.89 (95% CI: 1.69–4.94, I^2 = 83%, P = 0.0001; low). The elevated risk of VDD in individuals with T2DM remained statistically significant irrespective of sample size and age. Publication bias was detected through Egger's test (P = 0.038) and confirmed by the asymmetry observed in the funnel plots. However, the trim and fill method demonstrated that there was no substantial alteration in the effect size (pre-trim: 2.62 [1.85–3.70], post-trim: 2.379 [1.675–3.378]), indicating that publication bias had minimal impact on the outcomes of the meta-analysis. Please refer to Figure S4 for the trim and fill funnel plot.

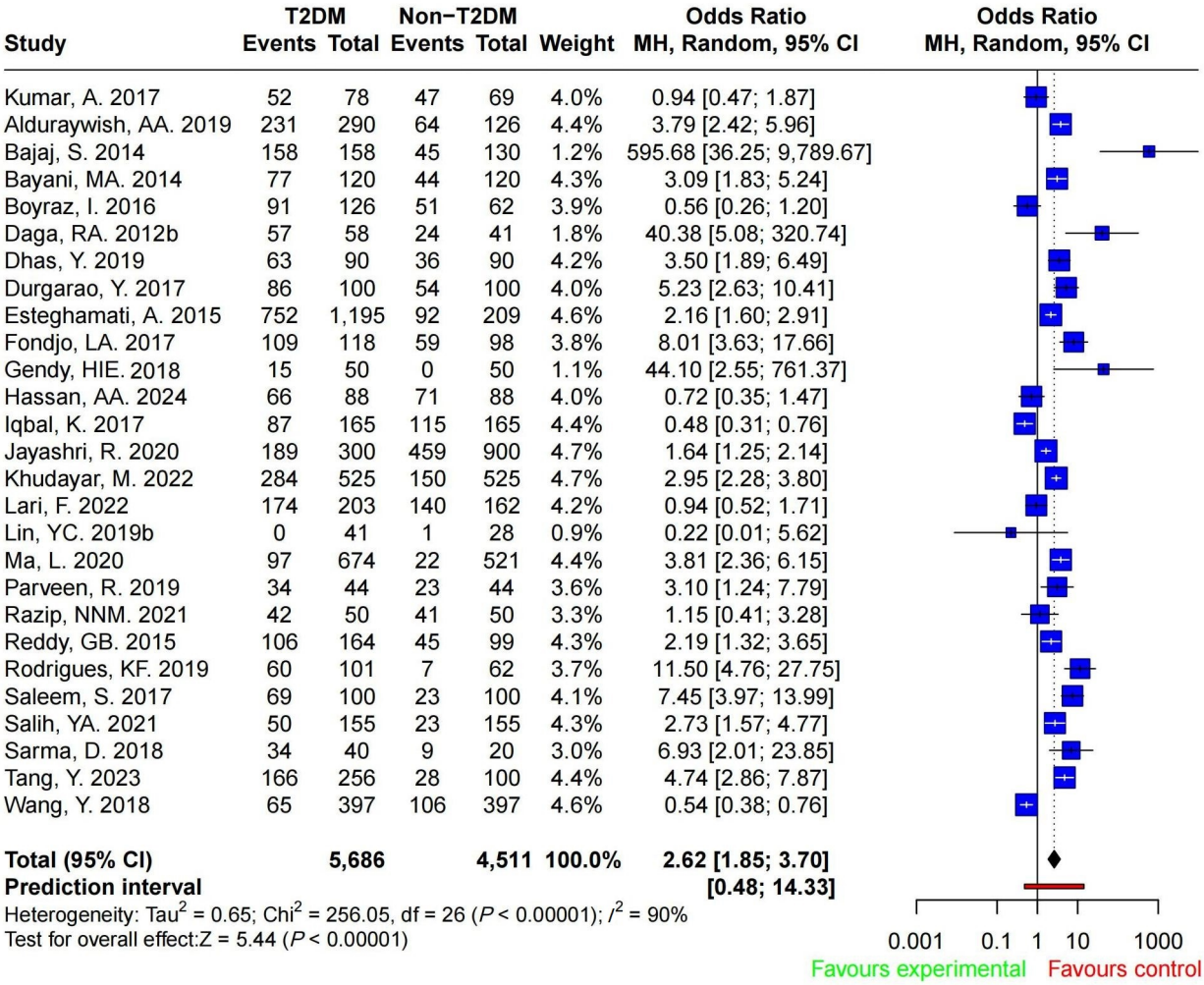

Figure 4. Comparison of the prevalence of VDD in patients with and without T2DM. CI: confidence interval; MH: Mantel-Haenszel; T2DM: type 2 diabetes mellitus; VDD: vitamin D deficiency

Discussion

The bidirectional relationship between diabetes mellitus and VDD has become a significant focus in metabolic disease research. Salih et al. [47] identified a substantial prevalence of vitamin D insufficiency and deficiency in individuals with T2DM (71%), especially in those with inadequate glycemic control and prolonged disease duration. This was established through a study involving 155 patients with T2DM and 155 non-exposed control subjects [47]. Similarly, Majeed et al. [62] observed a high prevalence of 25(OH)D deficiency among children and adolescents in the United Arab Emirates, with rates decreasing with age. Pittas et al. [71] reported that daily supplementation with 400 International Unit (IU) of vitamin D_3 did not significantly lower the risk of diabetes in high-risk populations not screened for VDD. Furthermore, they noted a higher prevalence of VDD in females compared to males, and a greater risk of VDD in obese individuals compared to those with normal weight [62]. Chen et al. [72] reported a negative correlation between serum 25(OH)D levels and the homeostatic model assessment of insulin resistance, specifically in females with VDD. This indicates a gender-specific effect of VDD on insulin resistance [72].

This study systematically examined the complex interaction between VDD and diabetes mellitus, including its subtypes (T1DM/T2DM), by analyzing 53 observational studies (n = 552,032). The findings revealed a 53% increased risk of T2DM (OR = 1.53) in individuals with VDD. This association is likely mediated by vitamin D's influence on pancreatic β-cell function and insulin signaling pathways. Studies show that vitamin D enhances insulin secretion by binding to vitamin D receptors (VDRs) on β-cells, which regulate insulin gene transcription [41]. VDD, meanwhile, promotes insulin resistance by upregulating inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin 6 (IL-6) and impairing glucose transporter type 4 (GLUT4) activity in skeletal muscle and adipose tissue [73, 74]. Conversely, the risk of VDD was elevated by 2.02-fold in patients with T1DM and 2.62-fold in those with T2DM. These results corroborate previous studies by Lucato et al. [75] and Yang et al. [76], underscoring the pivotal role of disrupted vitamin D metabolism in diabetes development. Importantly, this bidirectional relationship exhibited significant heterogeneity across populations. For instance, the risk of VDD was notably higher in T1DM patients in Asia (OR = 2.21) compared to European populations (OR = 1.65), while the risk in T2DM patients in Africa showed greater variability (OR = 4.75, 95% CI: 0.55–41.06). This suggests that genetic factors, environmental exposures, and healthcare access may contribute to these geographical differences [77]. Socioeconomic factors, including limited access to vitamin D-rich foods, healthcare disparities, and cultural practices (e.g., sun avoidance), may contribute to the observed geographic heterogeneity in VDD risk [78]. Polymorphisms in vitamin D metabolism genes, like the BsmI variant, are linked to a heightened risk of T1DM, especially prevalent in Asian populations, and may impact 25-hydroxylation and vitamin D binding [79]. Cultural practices, including skin-whitening norms and indoor lifestyles, along with high urban air pollution, further limit cutaneous vitamin D synthesis in these regions [78]. In contrast to Europe, where vitamin D management is often integrated into diabetes care, many Asian healthcare systems lack standardized screening and supplementation for VDD [78, 80].

Study design differences significantly influenced the results. Prospective cohort studies demonstrated a stronger effect of VDD on T2DM (I^2 = 66%), while retrospective case-control studies indicated a higher estimated risk of VDD in T2DM patients (OR = 2.71) but exhibited substantial heterogeneity (I^2 = 90%). The bidirectional analysis primarily relied on retrospective case-control studies (47 out of 53), whereas only 6 prospective cohort studies were included. It is important to highlight that the relationship between VDD and the development of T2DM was predominantly based on data from 5 prospective cohorts. Conversely, the reverse association, where diabetes mellitus leads to VDD, was mainly supported by retrospective data. This disparity in study designs could impact the ability to establish causality, given that case-control studies are susceptible to recall bias and residual confounding. Analysis of follow-up duration revealed a critical insight: the T2DM risk associated with VDD increased 1.66-fold (I^2 = 0%) when follow-up exceeded 5 years. This finding aligns with the 'cumulative metabolic damage' hypothesis by Schöttker et al. [81], which posits that persistent VDD can irreversibly impair islet function via chronic inflammation and oxidative stress. Conversely, short-term studies (< 5 years) showed negligible and non-significant effect sizes, implying that earlier vitamin D interventions might be necessary to prevent pathological processes.

The metabolic intricacy is further underscored by BMI stratification results: obese (BMI ≥ 30 kg/m^2) T2DM patients exhibit a lower VDD risk (OR = 5.21) compared to their normal-weight counterparts (OR = 7.68). This paradox may arise from vitamin D accumulation in subcutaneous adipose tissue in obese individuals, leading to seemingly lower circulating 25(OH)D levels [82], while lean patients might have an inherent defect in vitamin D absorption or metabolism. In obesity, excess subcutaneous adipose tissue may sequester lipid-soluble vitamin D, creating a "sink effect" that lowers circulating 25(OH)D levels despite adequate systemic availability [82]. This hypothesis is supported by studies showing serum vitamin D elevation following weight loss without supplementation [83]. The CI for the OR in the obese group was wide (0.08–332.64), with a non-significant *P* value (*P* = 0.44), possibly due to the small sample size (*n* = 2) or outliers. Interpretation of this result should be approached with caution. Conversely, the significantly increased VDD risk in lean T2DM patients suggests intrinsic metabolic defects, potentially involving genetic polymorphisms in vitamin D hydroxylating enzymes, such as *CYP2R1* variants impairing hepatic 25-hydroxylation [84], gut dysbiosis-mediated suppression of intestinal VDR expression [85]. These findings advocate for personalized supplementation strategies: higher doses to counteract adipose sequestration in obesity [86] and targeted therapies for absorption or metabolism defects in lean patients.

A complex interaction network links VDD and diabetes mellitus through multiple pathophysiological mechanisms. The high expression of the VDR in pancreatic β-cells and its regulatory role in insulin gene transcription underlie VDD's direct impact on insulin secretion [87–89]. Norman et al. [90] found that insulin secretion from pancreatic islets in rat models decreased by 40–50% in the VDD group. This function was partially restored after supplementation with 1,25(OH)$_2$D$_3$. In the endocrine pathway, vitamin D directly influences β-cell function by maintaining intracellular calcium homeostasis. It regulates L-type calcium channels and calcium-binding proteins, essential for glucose-stimulated insulin secretion [91]. Deficiency in vitamin D can disrupt calcium signaling, diminishing β-cell sensitivity to glucose and impairing insulin synthesis and release [91]. Furthermore, vitamin D activates VDR, enhancing GLUT4 expression and membrane transport capacity in skeletal muscle and adipose tissue [74, 91]. VDD leads to compromised glucose uptake in peripheral tissues. VDR gene polymorphisms, including BsmI, FokI, and ApaI loci, influence receptor activity [74]. Pro-inflammatory T helper 1 (Th1) and Th17 cells are critical in mediating autoreactivity against β-cells [92]. In animal models, 1,25(OH)$_2$D, the active form of vitamin D, enhances regulatory T (Treg) cell activity and inhibits Th17 and Th1 cells via VDR [93, 94]. VDD disrupts the balance between Th17 and Treg cells [95]. It reduces pro-inflammatory Th17 cell differentiation by inhibiting the STAT3/RORγt pathway, thereby decreasing cytokine-mediated autoimmune attacks, such as IL-17, on pancreatic islet β-cells, notably in T1DM. Conversely, deficiency leads to excessive IL-12 and IL-23 secretion by dendritic cells, promoting Th1/Th17 polarization and weakening Treg cells' immunosuppressive effects, exacerbating chronic low-grade inflammation [96]. This state upregulates inflammatory factors like TNF-α and IL-6 via nuclear factor kappaB (NF-κB) and Jun N-terminal kinase (JNK) pathways, disrupts insulin receptor substrate-1 (IRS-1) phosphorylation, and induces insulin resistance in skeletal muscle and adipose tissue [97]. Vitamin D supplementation can inhibit the NF-κB pathway, reducing pro-inflammatory factors, and may more effectively prevent and treat diabetes mellitus [73, 98], as demonstrated by Mohammad et al. [99] who observed a dose-dependent positive correlation between 25(OH)D levels and insulin sensitivity. Conversely, diabetes mellitus exacerbates VDD via several pathways: obesity-related fat accumulation decreases vitamin D bioavailability [82], diabetic nephropathy impairs 1,25(OH)$_2$D activation [100], and autonomic neuropathy limits outdoor activity, reducing skin synthesis of vitamin D.

While this study confirmed the robustness of its findings through sensitivity analyses and the trim and fill method, several limitations persist. The observational design cannot fully account for confounding factors like sunshine duration and dietary intake. Additionally, the predominance of studies from Asia (70%) may limit the global applicability of the results. Despite efforts to harmonize VDD diagnostic thresholds through data conversion, variations in 25(OH)D measurement methods across original studies may introduce residual bias. These limitations underscore the need for more prospective cohort studies, particularly standardized ones in underrepresented regions such as Africa and South America.

This study examines the integrated management of diabetes mellitus and VDD through clinical transformation. For Asian patients with T1DM and chronic VDD, routine clinical procedures should include regular monitoring of serum 25(OH)D levels, with intervention thresholds raised from the standard < 20 ng/mL to < 30 ng/mL. At the public health level, promoting vitamin D-fortified foods, such as dairy products, is suggested as an effective prevention strategy in regions with high prevalence, like South Asia and the Middle East. This study underscores the heightened risk of VDD in normal-weight T2DM patients, prompting clinicians to focus on lean individuals and tailor vitamin D supplementation plans. Gender differences, particularly in postmenopausal women with reduced estrogen affecting vitamin D binding protein function, should also be considered [72, 101]. Maintaining 25(OH)D levels at or above 25 ng/mL is recommended to enhance insulin sensitivity. Future research should investigate the metabolic benefits of VDR agonists in specific populations and determine the optimal timing and dosage of supplementation through randomized controlled trials to develop an evidence-based strategy for addressing the "metabolism-vitamin D disproportionation cycle".

Conclusion

This meta-analysis indicates a robust bidirectional link between diabetes mellitus and VDD. Individuals with VDD exhibited a 53% higher risk of developing diabetes, while those with T1DM and T2DM faced a 2.02-fold and 2.62-fold increased risk of VDD, respectively. Subgroup analyses highlighted geographic and metabolic variations, with elevated risks in Asian populations (OR = 2.21 for T1DM) and normal-weight T2DM patients (OR = 7.68 vs. obese: OR = 5.21). However, these findings should be interpreted with caution due to limitations such as significant heterogeneity (e.g., I^2 = 90% for VDD in T2DM), regional overrepresentation (70% of studies from Asia), and observational design constraints that preclude causal inference. The bidirectional analysis relied mostly on retrospective case-control studies (47 out of 53), which might lead to recall bias and residual confounding, especially in the diabetes mellitus to VDD pathway. Variations in 25(OH)D measurement methods and unmeasured confounds (sun, diet) may further bias the results. Routine screening of serum 25(OH)D levels in diabetic patients, especially in high-risk subgroups such as Asian individuals with T1DM and lean T2DM, is essential for guiding timely vitamin D supplementation. Vitamin D fortification programs for staple foods like dairy and cereals should be prioritized in regions with high deficiency rates, such as South Asia and sub-Saharan Africa. Incorporating 25(OH)D screening into diabetes management guidelines is advisable. Additionally, a thorough evaluation of the cost-effectiveness of vitamin D-fortified dairy products is warranted. Future research should focus on large, multi-regional prospective cohort studies with standardized vitamin D assays to confirm causality and determine clinical intervention thresholds.

Abbreviations

25(OH)D: 25-hydroxyvitamin D

BMI: body mass index

CI: confidence interval

CLIA: chemiluminescence immunoassay

GLUT4: glucose transporter type 4

GRADE: Grading of Recommendations, Assessment, Development, and Evaluation

IL-6: interleukin 6

NF-κB: nuclear factor kappaB

ORs: odds ratios

PI: prediction interval

T1DM: type 1 diabetes mellitus

T2DM: type 2 diabetes mellitus

Th1: T helper 1

TNF-α: tumor necrosis factor-alpha

Treg: regulatory T

VDD: vitamin D deficiency

VDRs: vitamin D receptors

Supplementary materials

The supplementary figures for this article are available at: https://www.explorationpub.com/uploads/Article/file/101438_sup_1.pdf. The supplementary tables for this article are available at: https://www.explorationpub.com/uploads/Article/file/101438_sup_2.pdf.

Declarations

Author contributions

HH: Writing—original draft, Writing—review & editing, Conceptualization, Methodology, Data curation, Formal analysis, Investigation, Resources, Supervision. SS: Data curation, Formal analysis, Investigation. DL: Formal analysis, Investigation. All authors read and approved the submitted version.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical approval

Not applicable.

Consent to participate

Not applicable.

Consent to publication

Not applicable.

Availability of data and materials

The original contributions presented in the study are included in the article/Supplementary materials. Further inquiries can be directed to the corresponding author.

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