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The association between the triglyceride-glucose index and vitamin D status: a systematic review and meta-analysis

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Abstract

Objective This study aims to explore the association between the triglyceride-glucose (TyG) index and vitamin D status to enhance our understanding of how vitamin D status relates to metabolic health and to provide evidence for the early diagnosis of vitamin D deficiency (VDD) using the TyG index.

Methods We conducted a comprehensive search in various databases, including PubMed, Web of Science, Embase, Cochrane Library, China National Knowledge Infrastructure (CNKI), China Biology Medicine disc, China Science and Technology Journal Database, and Wanfang Data to gather articles published from the inception of these databases until February 19, 2024. We assessed the quality of included studies using the Newcastle-Ottawa Scale (NOS) for case-control studies and the Agency for Healthcare Research and Quality (AHRQ) methodology checklist for cross-sectional studies. Statistical analyses in this study were conducted using conversion methods for non-standard data formats and consolidation techniques for combining multiple groups. The Fisher transformation method was used for correlation coefficients. We used a random-effects model considering the inherent clinical heterogeneity among the studies, and assessed statistical heterogeneity with the Cochrane Q test and I^2 statistic, complemented by subgroup analyses and sensitivity analysis.

Results Our meta-analysis selected a total of nine studies. The analysis revealed that patients with vitamin D deficiency (VDD group) exhibited a significantly higher TyG index than those without deficiency (no-VDD group), with a mean difference (MD) of 0.16 (95% CI: 0.10 to 0.23, $I^2 = 93\%$). This association was particularly pronounced among patients with type 2 diabetes (T2DM), showing an MD of 0.15 (95% CI: 0.05 to 0.26, $I^2 = 55\%$). Additionally, a negative correlation was observed between the TyG index and vitamin D levels, with a correlation coefficient (r) of -0.236 (95% CI: -0.310 to -0.159, $I^2 = 91\%$). Excluding each study sequentially in the sensitivity analyses did not significantly alter the outcomes.

Conclusions Our findings demonstrate a significant association between the TyG index and vitamin D status across diverse populations, including those with T2DM, subclinical hypothyroidism (SCH), and metabolic associated fatty liver disease (NAFLD). Our results reveal a notable disparity in the TyG index between vitamin D deficient and non-deficient groups, suggesting that vitamin D may play a critical role in metabolic health. These findings highlight the

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need for further research to explore the underlying mechanisms and clinical implications of vitamin D in the context of various metabolic disorders.

Keywords Triglyceride-glucose index, Vitamin D, Vitamin D deficiency, Metabolic health, Meta-analysis

Background

Vitamin D deficiency (VDD) has emerged as a major public health challenge globally, with an estimated 30–60% of the population, including children and adults, affected by either deficiency or insufficiency [1]. A multitude of studies have demonstrated that the impacts of VDD extend beyond the musculoskeletal system. Notably, it is associated with an elevated risk of various health conditions, including acute respiratory infections [2], autoimmune diseases [3], malignancies [4], cardiovascular diseases [5], depression [6], and diabetes [7]. These findings collectively highlight the critical role of addressing VDD in potentially mitigating a broad spectrum of health concerns. This significance is accentuated by the pivotal role of vitamin D in managing lipid metabolism, as it not only influences triglyceride levels but also impacts the overall lipid profile [8]. Furthermore, vitamin D's involvement in regulating inflammation and oxidative stress — both key contributors to metabolic disorders — adds another layer to its metabolic impact [9]. Emerging studies point to vitamin D's role in influencing insulin secretion and action, suggesting it may play a key role in modulating insulin resistance (IR) [10–12]. These findings highlight vitamin D's significant impact on enhancing glycemic control.

IR, a condition where peripheral tissues show a reduced response to insulin, plays a central role in the development of various metabolic diseases [13, 14]. The hyperinsulinemic-euglycemic clamp test, deemed the gold standard for assessing IR, is not commonly employed in clinical settings due to its cost and invasive procedure [15]. Currently, the Homeostasis Model Assessment-Estimated Insulin Resistance (HOMA-IR) index is often utilized to measure IR [16]. However, its reliance on fasting glucose and insulin levels limits its ability to reflect the dynamic interplay of insulin secretion and action. In recent years, the TyG index, calculated as ln(fasting triglycerides [mg/dL] × fasting glucose [mg/dL]/2), is gaining recognition for its effectiveness in predicting cardiovascular risk and other metabolic complications [17, 18], presenting a more accessible and less invasive option for evaluating IR in clinical and research settings. The TyG index is increasingly recognized for its association with lipid metabolism, indicating that higher TyG values correlate with dyslipidemia, including elevated triglycerides, increased low density lipoprotein cholesterol, and decreased high density lipoprotein cholesterol [19, 20]. Unlike traditional markers that focus solely on blood glucose or lipids, the TyG index integrates both parameters, offering a more holistic view of metabolic function, particularly in patients with type 2 diabetes mellitus (T2DM). As such, the TyG index stands out as a superior indicator in capturing the intricate interplay between glucose and lipid metabolism and reflecting the broader spectrum of metabolic health.

Considering the crucial roles of vitamin D status and the TyG index in glucose and lipid metabolism, it is rational to assess their relationship to overall metabolic health via the TyG index. Although there have been investigations into the relationship between the TyG index and vitamin D levels in various countries, a comprehensive summary of these findings is lacking. Recent studies have shed light on the negative correlation between vitamin D status and IR, suggesting that vitamin D supplementation may reduce the risk of IR [21–23]. However, most of these studies have focused on traditional markers like HOMA-IR, rather than the emerging TyG index. Therefore, our study aims to explore the association between the TyG index and vitamin D status, providing preliminary perspectives into the potential application of the TyG index as a diagnostic tool for VDD. The use of the TyG index for the early diagnosis of VDD is particularly relevant because routine clinical screening for vitamin D is not common, despite the increasing evidence of its significant impact. Furthermore, the TyG index is easily calculable and readily accessible, which supports our investigation into its potential integration into clinical practice. While the majority of research points to higher TyG indices in vitamin D deficient individuals, some studies report lower TyG indices in this group. Notably, the relationship between the TyG index and vitamin D status varies across different disease types, presenting a complex picture. These discrepancies highlight the necessity of a comprehensive systematic review and meta-analysis to unravel these complex association.

Materials and methods

This meta-analysis was conducted in strict adherence to the guidelines of the Meta-analysis of Observational Studies in Epidemiology (MOOSE) [24]. Additionally, the methodology aligns with the Cochrane guidelines for systematic reviews [25]. Furthermore, this study has been duly registered with the International Register of Prospective Systematic Reviews (PROSPERO) under the registration number CRD42024513774.

Search strategy

For this review, we meticulously searched several electronic databases, including PubMed, Web of Science, Embase, Cochrane Library, China National Knowledge Infrastructure (CNKI), China Biology Medicine disc (CBM), China Science and Technology Journal Database (VIP), and Wanfang Data, covering all records from their inception up to February 19, 2024. To identify relevant articles, we utilized a combination of MeSH terms and keywords such as "Vitamin D", "25(OH)D", "25-Hydroxyvitamin D" along with "triglyceride-glucose index", "triglyceride glucose index", "TyG index" and "TyG". This approach was designed to comprehensively capture original studies investigating the association between the TyG index and vitamin D status. The exact search strings used for each database are documented in Table S1.

Selection criteria and PECOS Framework

Two authors independently conducted a thorough evaluation and selection of pertinent studies, adhering to the predefined criteria: (1) study type: observational studies (including cohort, case-control, and cross-sectional studies) that report on the TyG index and vitamin D will be included; (2) study subjects: individuals who can be clinically diagnosed with vitamin D deficiency (VDD group) or identified as not having the deficiency (no-VDD group) based on established criteria including serum 25-hydroxyvitamin D levels below 20 ng/mL or 50 nmol/L [26], with no age restrictions for participants; and (3) study index: data on the TyG index and vitamin D status must be recorded completely.

Exclusion criteria: (1) studies without primary data: reviews, editorials, commentaries, and studies without original data (such as meta-analyses); (2) duplicate publications or overlapping study subjects; (3) studies that do not report both the TyG index and vitamin D status or do not provide sufficient information to calculate these values; and (4) preclinical studies (in vitro or animal experiments).

In the PECOS framework for this meta-analysis, the Population consisted of individuals with metabolic conditions such as T2DM, subclinical hypothyroidism (SCH), and metabolic associated fatty liver disease (MAFLD) from diverse regions including China, India, Mexico, and Ukraine, reflecting the global prevalence and pathophysiological links through insulin resistance. The Exposure under investigation was vitamin D status, categorized based on serum levels with deficiency defined as <20 ng/mL and sufficiency as ≥ 20 ng/mL. The Comparison was between those with vitamin D deficiency and those with sufficient levels across the varied metabolic conditions. The Outcome of interest was the TyG index, a measure of insulin resistance and metabolic function, with secondary outcomes examining the correlation between vitamin D levels and the TyG index. The meta-analysis synthesized results from Study Designs including case-control and cross-sectional studies, providing a comprehensive assessment of the association between vitamin D status and metabolic markers.

Data extraction

From the included articles, data extraction was independently performed by two authors, focusing on the following details: (1) study characteristics, including first author, year of publication, nationality, study design; (2) basic characteristics of the individuals, including sample size (n), mean age, sex ratio, the TyG index and presence or absence of VDD. In addition, we extracted correlation coefficients [27] to further assess the association between the TyG index and vitamin D levels. When reporting Spearman correlation coefficients, we converted them to Pearson correlation coefficients using a well-established method outlined in prior research [28]. We also extracted the area under the curve (AUC) from studies that reported AUC for the diagnosis of VDD.

Quality assessment

To evaluate the quality in the included studies, the two authors utilized distinct assessment tools based on the type of each observational study. The Newcastle-Ottawa Scale (NOS) was employed for assessing case-control studies [29], while the Agency for Healthcare Research and Quality (AHRQ) methodology checklist (www.ncbi.nlm.nih.gov) was applied to cross-sectional studies. Studies were categorized into low (<5 stars), medium (5–7 stars), or high quality (>7 stars) based on the star rating system. The AHRQ methodology comprises an eleven-item checklist, with the quality of studies ranked as low ($<30\%$ "yes" responses), medium (30-60% "yes"), or high quality ($>60\%$ "yes").

Results of interest

In our meta-analysis, we designated the disparity in the TyG index between VDD group and no-VDD group as the primary outcome. Additionally, we identified the correlation between the TyG index and vitamin D levels as the secondary outcome.

Statistical analysis

All the statistical computations and analyses in this study were conducted using RevMan 5.3 and Stata 18. Whenever the data were presented as median and interquartile range (IQR) or median and range for any required variables, we derived the mean and standard deviation using the conversion methods proposed by Luo et al. [30] and Wan et al. [31]. In instances where it was necessary to combine multiple groups with their respective

n, means, and standard deviations (SD), we employed the consolidation techniques outlined by Higgins et al. (training.cochrane.org/handbook). Given that the TyG index values were continuous and all metrics were calculated in uniform data units, we integrated effect sizes by computing the mean difference (MD), SD, and the corresponding 95% confidence interval (95% CI). Recognizing the inherent clinical heterogeneity among the studies, we opted for the random-effects model as the most suitable approach for summarizing the effect measures. The statistical heterogeneity of individual outcome studies was assessed using the Cochrane Q test [32] and the I^2 statistic [33]. To delve into the clinical heterogeneity, we conducted subgroup analyses based on different diseases. Sensitivity analysis was also employed to gauge the robustness of our meta-analysis findings. Moreover, to handle correlation coefficient values, we initially applied the Fisher transformation method for conversion, followed by a meta-analysis using the generalized inverse variance model to derive a summary of Fisher Z values. These summary Z-values were then converted back to r-values using standard formulae. We did not assess publication bias because the Cochrane Handbook of Interventional System Reviews (www.cochranehandbook.org) states that publication bias studies with funnel plots are not required when there are fewer than 10 studies. Differences were considered statistically significant at P-values less than 0.05.

In our meta-analysis examining the association between the TyG index and vitamin D status, we have included both case-control and cross-sectional studies. Despite the differences in their designs, both types of studies offer consistent and comparable outcome measures relevant to our research: [1] the TyG index in individuals with and without vitamin D deficiency, and [2] the correlation coefficients between vitamin D levels and the TyG index. Both study designs are observational and share a common methodological framework, involving either prospective recruitment of participants or use of pre-existing cohorts, followed by laboratory measurements. To ensure a valid synthesis of results, we employed a rigorous methodology that includes design-specific quality assessment tools, a random-effects model to account for between-study variability, and sensitivity and subgroup analyses to address heterogeneity and potential biases. Furthermore, pooling these studies is justified by the fact that both study types aim to assess similar underlying relationships and outcomes, thereby allowing for a comprehensive understanding of the association between the TyG index and vitamin D status. By integrating results from different study designs, we enhance the robustness and generalizability of our findings, and provide a more complete evaluation of the evidence base. This methodological approach aligns with established practices in meta-analysis and maximizes the utility of available data.

Results

Literature search

Following our explicitly defined search strategy, we initially identified 393 publications. After removing duplicates, 318 potentially relevant articles were shortlisted. A further review based on titles and abstracts led to the exclusion of 304 publications that did not meet the study criteria. We then conducted a comprehensive full-text assessment of the remaining 14 articles. Subsequently, nine studies [34–42] that fulfilled our stringent inclusion criteria were incorporated into the meta-analysis. The detailed flow of the literature search and selection process is graphically represented in Fig. 1.

Basic information of included studies

In this meta-analysis, ultimately nine studies were ultimately selected for inclusion, with four [36, 38, 40, 41] originating from China, three [34, 37, 39] from India, one [42] from Mexico, and one [35] from Ukraine. These comprised seven [35–38, 40–42] cross-sectional and two [34, 39] case-control studies. Collectively, they encompassed a participant pool of 5,949 individuals with VDD and 9,917 without, facilitating the comparison of the TyG index. Additionally, a total of 14,702 participants were involved in analyzing the correlation between the TyG index and vitamin D levels, using either the Spearman or Pearson correlation coefficient. Among these studies, three unique studies focused on populations with unspecified disease status: 10,167 Indian adolescents [37], 3,143 Euthyroid adults [41], and 1,904 Mexican adults [42], while the rest targeted mostly middle-aged and older adults with metabolic diseases, including four studies [34–36, 38] on T2DM, one [40] on MAFLD, and one [39] on SCH. The baseline characteristics of these studies are visually summarized in Table 1.

Quality evaluation of included studies

For assessing the quality of the seven cross-sectional studies included in our meta-analysis, we applied the AHRQ methodology checklist, with the detailed evaluations presented in Table 2. Among these, five studies [36, 38, 40–42] were categorized as high quality, while two [35, 37] were deemed medium quality. The quality assessment of the two case-control studies was conducted using the NOS, as detailed in Table 3, with both studies achieving a high-quality rating [34, 39]. Collectively, the studies incorporated into this meta-analysis exhibited a commendably high level of quality.

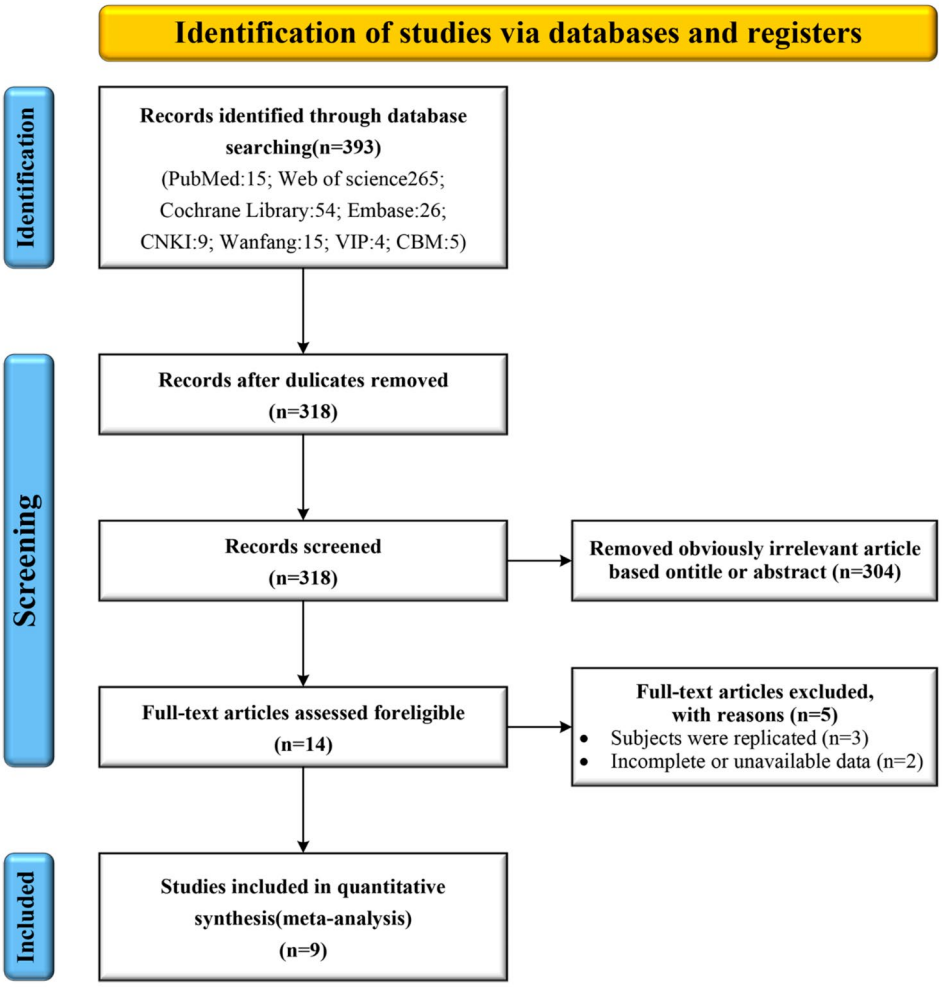

Fig. 1 PRISMA flow diagram of literature search

Meta-analysis of the TyG index in VDD group and no-VDD group

In our meta-analysis, eight of the included studies reported on the TyG index in both VDD group (n=5,949) and no-VDD group (n=9,917). The aggregated data revealed a significantly higher TyG index in the VDD group compared to the no-VDD group (MD=0.16, 95% CI: 0.10 to 0.23, P<0.00001), as illustrated in Fig. 2. Significant heterogeneity was detected (I^2=93%, P<0.00001); therefore, we performed a subgroup analysis based on different disease types. The results, depicted in Fig. 3, showed distinct variances in the TyG index between the T2DM subgroup (MD=0.15, 95% CI: 0.05 to 0.26, P=0.004) and other metabolic disease subgroups (MD=0.27, 95% CI: -0.07 to 0.62, P=0.12). The heterogeneity in the T2DM group was somewhat reduced (I^2=55%), but remained high in the other metabolic diseases group (I^2=98%). Additionally, the subgroup with unclear disease status demonstrated a mean difference of 0.06 (95% CI: 0.05 to 0.07) with a P-value less than 0.00001 and no heterogeneity (I^2 = 0%). The stability of our results was affirmed through sensitivity analysis, depicted in Fig. 4. This analysis demonstrated that the exclusion of individual studies did not lead to any significant changes, thereby confirming the robustness of our findings.

Meta-analysis of the relationship between the TyG index and vitamin D status

Within the included studies, eight [34–40, 42] examined the relationship between the TyG index and vitamin D levels, with Pearson or Spearman correlation coefficients computed from the data. A meta-analytical summary of this relationship was performed using Fisher's z transformation. As illustrated in Fig. 5, the meta-analysis yielded a Fisher's Z value of -0.24 (95% CI: -0.32 to -0.16, I^2=91%), indicating a significant negative correlation between the TyG index and vitamin D levels. This was further supported by a total r-value of -0.236 (95% CI: -0.310 to -0.159). Subsequently, a subgroup

Table 1 Characteristics of the included studies

Study	Country	Research type	Characteristics of participants	Number of participants	Age (years)	Male (%)	TyG index in VDD group			TyG index in no-VDD group			Spearman correlation	Pearson correlation
							Mean1	SD1	n1	Mean2	SD2	n2		
Dhas, [34]	India	case-control	T2DM patients (*n*=90) Controls (*n*=90)	180	T2DM: 37.97±6.14 Controls: 41.83±5.91	56.67%	T2DM 9.05 Controls 8.39	T2DM 0.56 Controls 0.39	T2DM 63 Controls 36	T2DM 9.11 Controls 8.42	T2DM 0.68 Controls 0.49	T2DM27 Controls 54	ρ=-0.272	
Aludwan, [35]	Ukraine	cross-sectional	T2DM patients	109	61.46±9.73	NA	5.17	0.41	60	5.08	0.31	49		*r*=-0.145
Paredez, [42]	Mexico	cross-sectional	Mexican Adults	1904	48.59 (36.82, 55.80)	30.57%							*r*=-0.213	
Jia, [36]	China	cross-sectional	T2DM patients	592	58.4±4	63.18%	9.23	0.75	405	9.06	0.74	187		*r*=-0.13
Mustafa, [37]	India	cross-sectional	Indian adolescents	10167	adolescents (10-19)	51.40%	4.51	0.24	2505	4.45	0.24	7662		*r*=-0.14
Xiang, [38]	China	cross-sectional	T2DM patients	1034	62.0±11.14	60.06%	9.21	0.77	632	8.96	0.69	402	*r*=-0.172	
Mahat, [39]	India	case-control	SCH patients (*n*=75) Controls (*n*=75)	150	SCH: 45.36±11.43 Controls: 44.73±10.21	44%	SCH 9.09	SCH 0.05	SCH 33	SCH 8.99	SCH 0.06	SCH 42	SCH ρ=-0.392	
Liu, [40]	China	cross-sectional	MAFLD patients	566	52 (42,60)	59.17%	9.11	0.53	366	8.66	0.48	200	*r*=-0.434	
Zhou, [41]	China	cross-sectional	Euthyroid Adults	3143	47.0±11.9	64%	8.71	0.65	1849	8.63	0.60	1294		

T2DM, type 2 diabetes mellitus; SCH, subclinical hypothyroidism; MAFLD, metabolic associated fatty liver disease; NA, not available

analysis based on different disease types was conducted. As shown in Fig. 6, in both T2DM group (Fisher's Z= -0.16, 95% CI: -0.21 to -0.12) and the group with other metabolic diseases (Fisher's Z = -0.48, 95% CI: -0.56 to -0.40), a significant negative correlation between the TyG index and vitamin D levels was observed. Moreover, statistical heterogeneity was notably reduced in both groups (I^2=0). Additionally, in the subgroup with unclear disease status, a Fisher's Z value of -0.20 (95% CI: -0.28 to -0.12, I^2 = 86%) was found. Sensitivity analysis further validated the stability of these findings, with the results presented in Table S2. Excluding the studies of Dhas [34], Aludwan [35], Jia [36], Mustafa [37], Xiang [38], Mahat [39], Liu [40], and Paredez [42] individually, the Fisher's Z values with 95% CIs were consistently significant, ranging from −0.32 to -0.15, -0.34 to -0.17, -0.35 to -0.17, -0.36 to -0.17, -0.35 to -0.16, -0.31 to -0.15, -0.24 to -0.14, and −0.35 to -0.15, respectively, confirming the robustness of our outcomes.

AUC for the prediction of VDD

In our comprehensive analysis, we focused on evaluating the AUC values of the TyG index as presented in various studies. This assessment was aimed at determining the index's efficacy in predicting VDD across different medical conditions. Our findings, as detailed in Table 4, shed light on the predictive value of the TyG index in various contexts. This analysis highlights the TyG index as a significant predictor of VDD, with varying degrees of accuracy across different patient cohorts. The study underscores the TyG index's potential utility in clinical settings, particularly for early detection and management of VDD in diverse conditions.

Discussion

Comparison with existing research results

Current research trends are focusing on vitamin D's impact on metabolic processes. Studies have identified that vitamin D influences insulin secretion and activity by acting on pancreatic β-cells and tissues responsive to insulin, such as muscle and adipose tissue [43–45]. However, the relationship between vitamin D status and IR is complex and not universally agreed upon. Rasouli et al. [46] reported supplementing with vitamin D3 for a continuous period of 24 months did not improve insulin sensitivity in patients with prediabetes. This may be attributed to the study's use of HOMA-IR for assessing IR instead of the more precise hyperinsulinemic-euglycemic clamp test, implying that the choice of IR assessment technique could impact experimental outcomes [47].

In T2DM, where IR is a core issue, vitamin D enhances insulin sensitivity and has anti-inflammatory effects, potentially mitigating the disease's progression [48]. Moreover, VDD is also linked to dysfunctions in

Table 2 Quality assessment of cross-sectional studies with AHRQ methodology checklist

Author (year)	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	Percent
Aludwan [35]	Y	Y	N	U	Y	Y	N	Y	N	U	U	5/11(45%)
Paredez [42]	Y	Y	Y	Y	Y	N	N	Y	Y	N	U	7/11(64%)
Jia [36]	Y	Y	Y	Y	Y	Y	N	Y	N	Y	U	8/11(73%)
Mustafa [37]	Y	Y	Y	U	U	N	N	Y	U	Y	U	5/11(45%)
Xiang [38]	Y	Y	Y	Y	Y	N	N	Y	Y	U	U	7/11(64%)
Liu [40]	Y	Y	Y	Y	Y	N	N	Y	Y	N	U	7/11(64%)
Zhou [41]	Y	Y	Y	Y	Y	Y	N	Y	N	Y	U	8/11(73%)

AHRQ, Agency for Healthcare Research and Quality; Y, Yes; N, No; U, Unclear

[1] Define the source of information (survey, record review); [2] List inclusion and exclusion criteria for exposed and unexposed subjects (cases and controls) or refer to previous publications; [3] Indicate time period used for identifying patients; [4] Indicate whether or not subjects were consecutive if not population-based; [5] Indicate if evaluators of subjective components of study were masked to other aspects of the status of the participants; [6] Describe any assessments undertaken for quality assurance purposes (e.g., test/retest of primary outcome measurements); [7] Explain any patient exclusions from analysis; [8] Describe how confounding was assessed and/or controlled; [9] If applicable, explain how missing data were handled in the analysis; [10] Summarize patient response rates and completeness of data collection; [11] Clarify what follow-up, if any, was expected and the percentage of patients for which incomplete data or follow-up was obtained

Table 3 Quality assessment of the newcastle-ottawa scale for case-control studies

Author (year)	Selection	Comparability	Outcome/ Exposure	NOS score
Dhas [34]	★★★★	★	★★★	8
Mahat [39]	★★★★	★	★★★	8

★: The NOS consists of eight items categorized into three aspects. Each numbered item can score one star if the study is eligible. A maximum of four stars can be awarded for selection, two stars for comparability, and three stars for outcome or exposure

pancreatic β-cell function, crucial for maintaining normal glucose levels. Hence, VDD might exacerbate IR and glucose metabolism disorders in T2DM. In the context of T2DM, the TyG index is not just a measure for VDD but also a significant indicator of the disease's metabolic complications. The TyG index is useful in T2DM because it provides insights into the interplay between vitamin D status and the metabolic dysfunctions typical of diabetes. This offers a more comprehensive approach to managing the condition. The associations between vitamin D and other metabolic diseases such as NAFLD and SCH further highlight the multifaceted role of vitamin D in metabolic health. Studies have shown that lower vitamin D levels are associated with higher NAFLD prevalence and severity, possibly due to vitamin D's effects on insulin sensitivity, lipid metabolism, and anti-inflammatory properties [49, 50]. SCH, characterized by an elevated thyroid-stimulating hormone (TSH) level with normal thyroid hormone levels, has been linked to various metabolic derangements, including IR and dyslipidemia [51]. Emerging evidence suggests that vitamin D plays a role in thyroid function, with deficiency associated with an increased risk of subclinical hypothyroidism [52].

VDD affects glucose and lipid metabolism through several mechanisms. Vitamin D acts as a steroid hormone, binding to the vitamin D receptor (VDR) in tissues like muscle, liver, and adipose tissue. This activation improves insulin sensitivity by increasing the expression of insulin receptor substrates and glucose transporters, such as GLUT4, enhancing cellular glucose uptake. VDD impairs these processes, leading to insulin resistance [53]. Additionally, vitamin D regulates lipid metabolism by influencing peroxisome proliferator-activated receptors (PPARs), especially PPAR-γ, which affects lipid synthesis and breakdown. A deficiency in vitamin D can disrupt PPAR-γ activity, leading to lipid accumulation and conditions like NAFLD [54]. Vitamin D also has

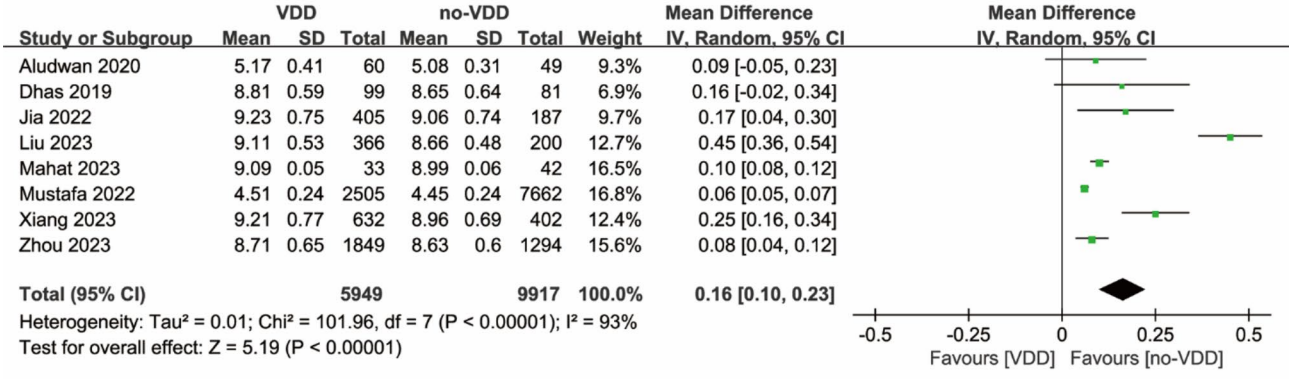

Fig. 2 Forest plot of meta-analysis of differences in the TyG index between VDD group and no-VDD group

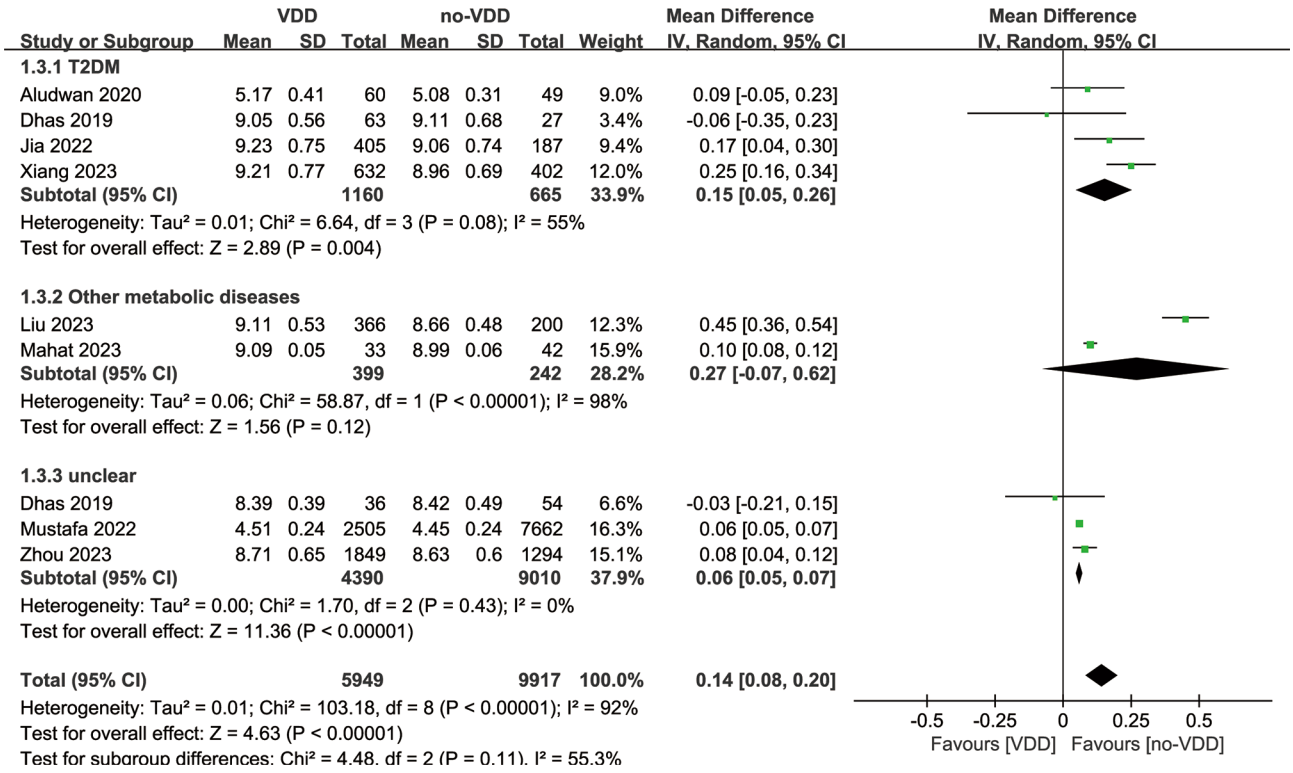

Fig. 3 Forest plot of subgroup meta-analysis of differences in the TyG index between individuals with different diseases

anti-inflammatory effects, helping to control inflammatory cytokines like TNF-α and IL-6, which contribute to insulin resistance and metabolic syndrome [55]. Thus, adequate vitamin D levels are crucial for maintaining glucose and lipid balance and preventing metabolic disorders.

In clinical practice, vitamin D levels are not routinely included in standard examinations, often leading to the neglect of this essential health parameter. Given the elevated incidence of VDD, such oversight is concerning. The TyG index, due to its strong relationship with metabolic health, is gaining prominence as an easily accessible biomarker in clinical settings. Patients with higher TyG levels may face an increased risk of VDD. Therefore, utilizing the TyG index as a predictive marker for VDD and intervening early to prevent complications are paramount. Vitamin D absorption is influenced by lipid metabolism due to its fat-soluble nature [56]. The TyG index, closely linked to lipid metabolism, might explain its predictive power for VDD. In the three studies we included in our meta-analysis [38–40], AUC for the TyG index used in predicting VDD was close to 0.7, suggesting a certain level of precision. In the research conducted by Xiang et al. [38], multivariate logistic regression results showed an increasing trend in VDD prevalence across the TyG index quartiles, with the Q1 quartile as the reference. This trend persisted even after adjusting for various confounders, with all results being significant (P all <0.05). This underscores the value of the TyG index in the early diagnosis of VDD in the clinical setting.

Our meta-analysis confirms a significant negative correlation between the TyG index and vitamin D status, indicating that higher TyG indices may suggest VDD. However, it's important to note that our study primarily focused on establishing this general relationship, rather than exploring its variations across different demographic groups. While this aspect extends our findings and is suggested by existing research, it was not deeply investigated due to data constraints. This limitation underscores the need for more comprehensive future studies that can conduct detailed subgroup analyses. Jia et al. [36] discovered a distinct negative correlation between serum vitamin D levels and the TyG index in male patients with T2DM, a pattern not observed in female patients. Xiang et al.'s research [38] further highlighted these gender disparities, revealing an increased risk of VDD across all quartiles of the TyG index in males, while in females, this risk was significant only in the highest quartile. Furthermore, Xiang et al. [38] identified a strong and noteworthy association between the TyG index and VDD among participants over 65 years of age. In contrast, this association was not evident in younger participants, suggesting that the TyG index could serve as an effective indicator of VDD prevalence particularly in the elderly population

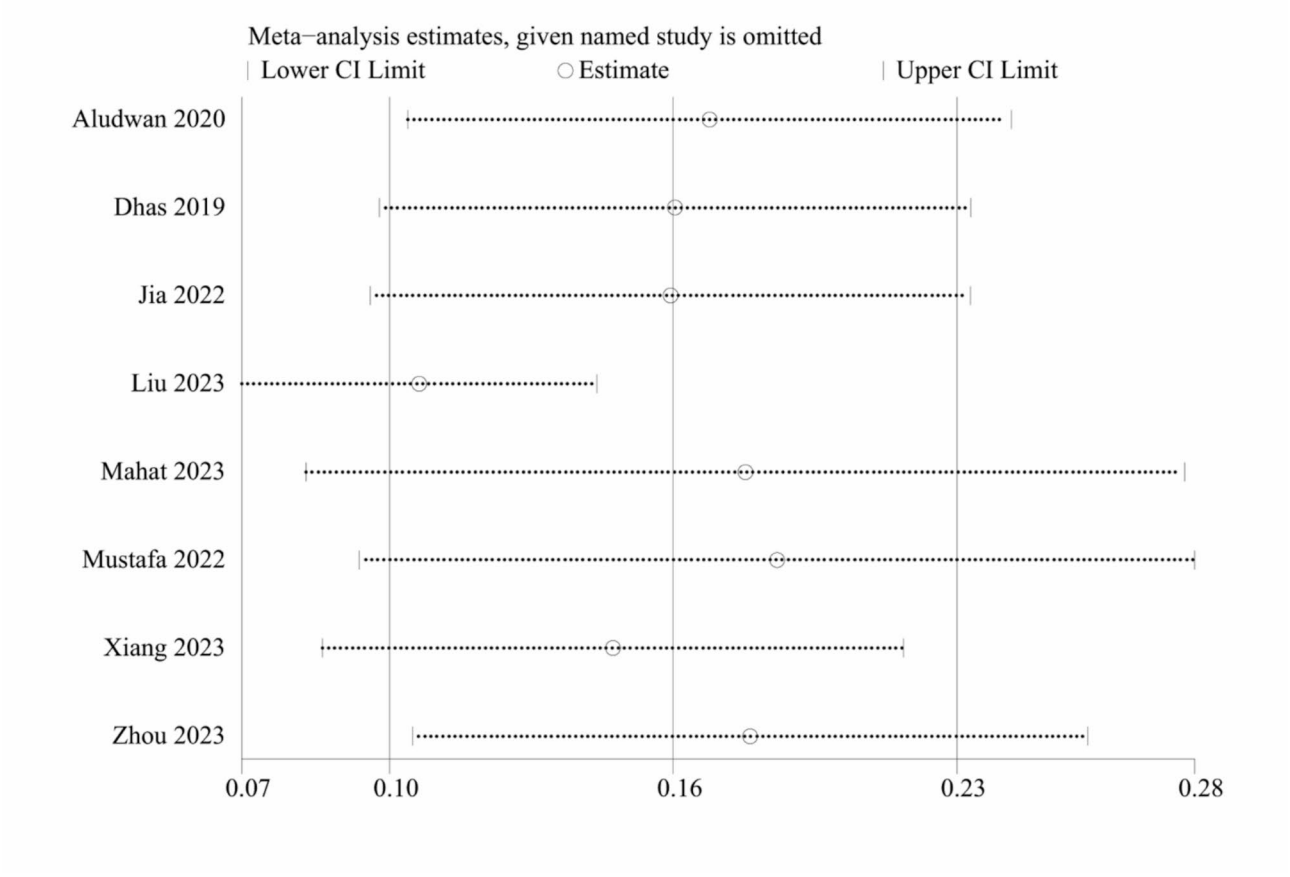

Fig. 4 Sensitivity analysis of differences in the TyG index in VDD group and no-VDD group

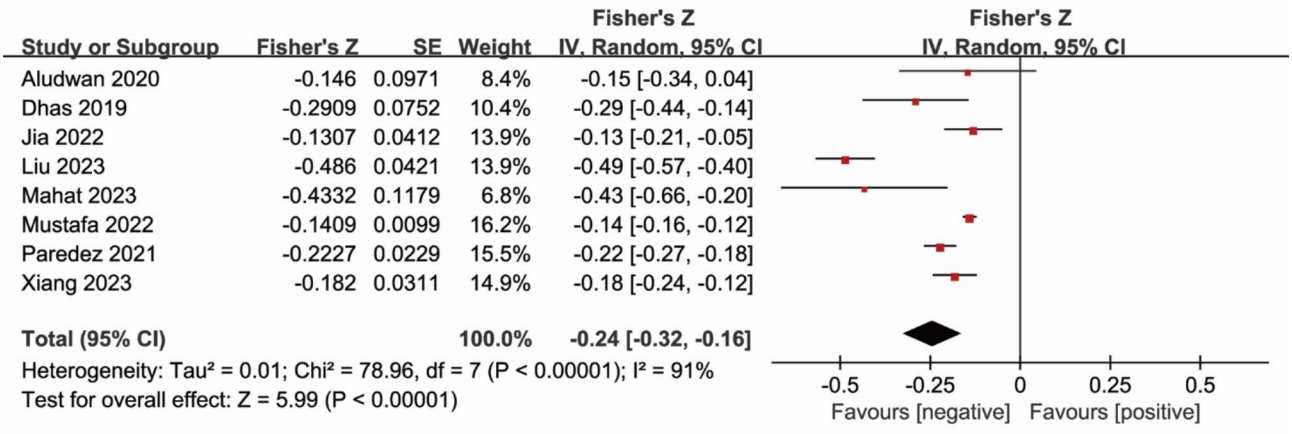

Fig. 5 Forest plot of meta-analysis of the relationship between the TyG index and vitamin D levels

with T2DM. These findings collectively underscore the potential of the TyG index as a differential marker for assessing vitamin D status in diverse demographic groups.

Strengths and limitations

Our study exhibits unique strengths. First, it presents a groundbreaking analysis that systematically reviews and examines the relationship between the TyG index and vitamin D status. Second, our comprehensive literature search has yielded extensive and pertinent findings, ensuring a robust and wide-ranging foundation for our analysis. Third, despite there is some heterogeneity in the results, the predominantly moderate to high quality of the included studies lends considerable confidence to our findings. Finally, our subgroup analysis, focusing on the

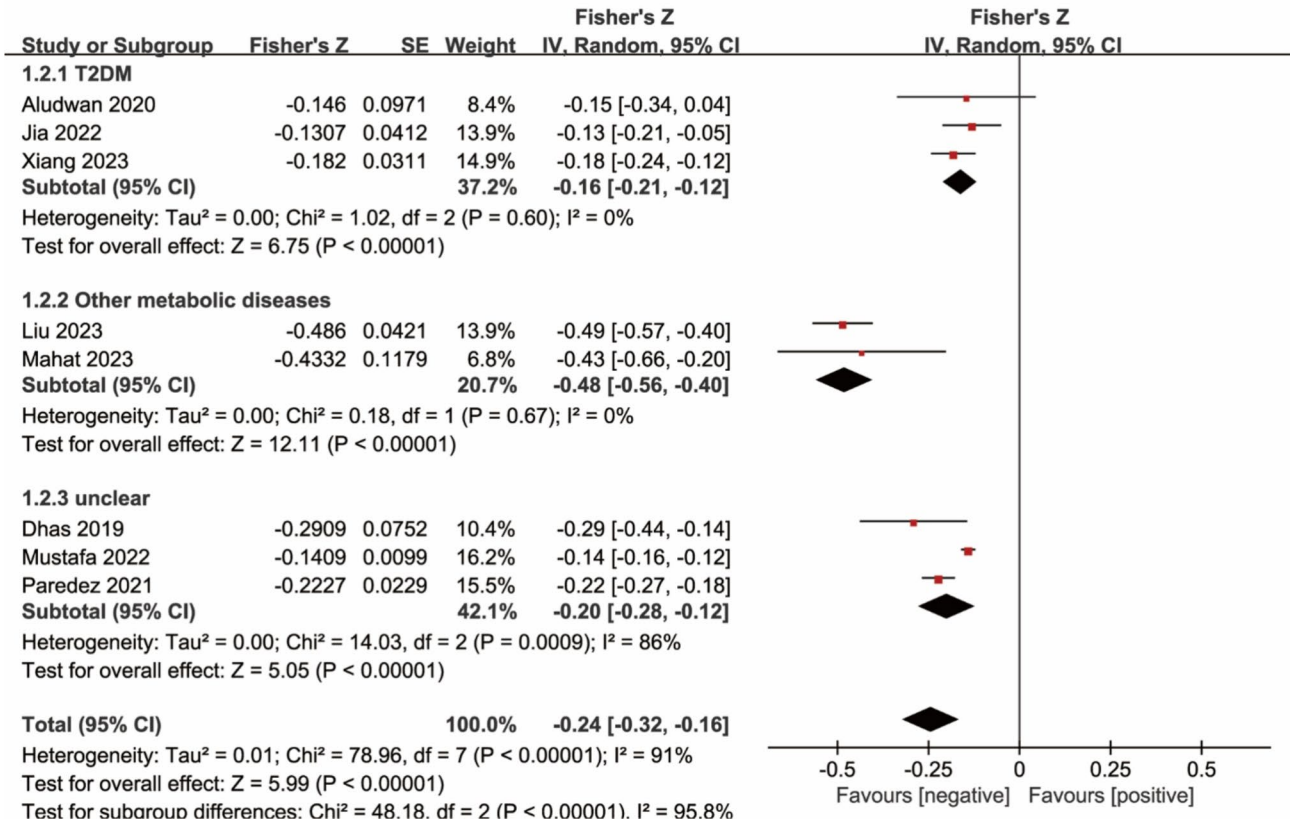

Fig. 6 Forest plot of subgroup meta-analysis of differences in the relationship between the TyG index and vitamin D levels in individuals with different diseases

Table 4 Comparative analysis of the TyG index's predictive accuracy for VDD across different studies

Study	Condition	AUC	95% CI	Youden's Index	*P*-Value	Optimal Cut-off Value	Sensitivity (%)	Specificity (%)
Xiang, [38]	VDD in T2DM	0.647	—	0.331	< 0.001	9.03	75.0	41.9
Liu, [40]	VDD in MAFLD	0.744	0.701 to 0.787	—	< 0.001	8.750	76.5	64.5
Mahat, [39]	VDD in SCH	0.759	0.650 to 0.868	0.38	< 0.001	4.86	78.8	59.5

association of the TyG index with vitamin D status across different disease types, has further strengthened the reliability of our conclusions.

However, our study faces several limitations. First, our study encountered significant heterogeneity across the included dataset, which we addressed with detailed subgroup analyses based on different disease types. This approach notably reduced heterogeneity within the T2DM group but heterogeneity remained pronounced in other metabolic disease groups. This increased heterogeneity is mainly due to the group consisting of only one study each on SCH and MAFLD. The substantial divergence between these two conditions, along with the scarcity of studies, hindered further analysis to pinpoint specific sources of heterogeneity. In addition to the challenges mentioned, the heterogeneity observed in our study might also stem from the geographical and demographic diversity of the study populations. Different regions may exhibit unique environmental and genetic factors that affect disease manifestation and response to treatment, contributing to variability in outcomes. Furthermore, the age, gender, and ethnic composition of the populations studied could introduce additional layers of heterogeneity, particularly if these aspects are not evenly distributed across studies. Additionally, the variability in the stage or severity of diseases at the time of study enrollment could lead to different responses, impacting the overall results. Another potential source of heterogeneity is the differing lengths of follow-up among studies, which might affect the observed effects of interventions. Addressing these sources comprehensively would require more granular analyses and possibly incorporating meta-regression to explore these moderators' impacts. Second, the observational nature of the included studies limits our ability to establish a definitive causal relationship between the TyG index and vitamin D status. Third, another constraint in our study is the relatively small number of studies that met our inclusion criteria,

limiting the depth of our analysis. Despite these limitations, our study adds statistical power by pooling results from individual studies, allowing for stronger conclusions. The total number of subjects in our analysis is large enough to support these conclusions. While acknowledging these limitations, our study still provides valuable insights into the relationship between the TyG index and vitamin D status, emphasizing the need for further research, including cohort and experimental studies, to explore the causal relationship between the TyG index and vitamin D status more comprehensively.

Despite the lack of detailed clarity on participant conditions and states in studies by Dhas, Mustafa, and Paredez, the findings of this meta-analysis remain significant, offering valuable insights into the relationship between vitamin D status and metabolic health. Each study employed rigorous methodologies, including well-defined inclusion and exclusion criteria, which enhance the reliability of their results. For instance, Dhas et al. ensured that participants in the control group were free from chronic conditions such as type 2 diabetes and hypertension, while Mustafa et al. focused on a large adolescent population, providing a broad perspective on vitamin D levels across different age groups. Furthermore, the studies utilized consistent methodologies for measuring vitamin D levels and the TyG index, facilitating comparability and strengthening the validity of our pooled analysis. The substantial sample sizes across these studies contribute to the robustness of our findings, allowing for more powerful statistical analysis and the potential for generalization to wider populations. However, the ambiguity around participants' precise health statuses in certain studies challenges definitive interpretation of the results. Nevertheless, the overarching trends observed suggest a meaningful association between vitamin D deficiency and metabolic disorders, underscoring the importance of regular vitamin D assessment in clinical practice. In conclusion, while the limitations regarding participant characterization should be acknowledged, the strengths of the studies in terms of methodological rigor and large sample sizes highlight the relevance of our findings and the need for further research to elucidate the causal relationships involved. Future studies should aim to provide more detailed participant profiles to enhance the understanding of how vitamin D status influences metabolic health across different populations.

Implications for Practice and Research

Our meta-analysis highlights a critical gap in current clinical practices, where the regular assessment of vitamin D levels is often overlooked. This oversight can lead to underdiagnosis and exacerbation of metabolic disorders, emphasizing the need to incorporate vitamin D evaluation into routine clinical assessments. The TyG index is probably emerging as a crucial tool in identifying and managing metabolic disorders, especially in the early diagnosis of VDD. While our study provides foundational insights, extensive research is needed to explore these connections in diverse populations. Additionally, these results highlight the need for public health strategies that prioritize awareness and regular screening for vitamin D levels, particularly in high-risk groups, to improve overall metabolic health outcomes.

Conclusion

Our meta-analysis examined the association between the TyG index and vitamin D status across various populations with differing metabolic conditions, including T2DM, SCH, and MAFLD. Our findings indicate a significant disparity in the TyG index between VDD and no-VDD groups, suggesting that vitamin D status may play a crucial role in metabolic health. Moreover, the correlation between the TyG index and vitamin D levels was observed across diverse populations, highlighting the potential relevance of vitamin D in metabolic regulation beyond T2DM. Given the heterogeneity of the included studies, further research is warranted to elucidate the underlying mechanisms and to determine the clinical implications of these findings in different populations. Overall, our results underscore the importance of considering vitamin D status in the assessment and management of metabolic disorders, and they call for more comprehensive studies to explore this association in varied clinical contexts.

Abbreviations

TyG	Triglycerides and Glucose
T2DM	Type 2 diabetes
IR	Insulin resistance
VDD	Vitamin D deficiency
MOOSE	Meta-analysis of Observational Studies in Epidemiology
PROSPERO	Prospective Systematic Reviews
CNKI	China National Knowledge Infrastructure
CBM	China Biology Medicine disc
VIP	China Science and Technology Journal Database
TG	Triglyceride
AUC	Area under the curve
NOS	Newcastle-Ottawa Scale
ANRQ	Agency for Healthcare Research and Quality
IQR	Interquartile range
SD	Standard deviations
MD	Mean difference
95% CI	95% confidence interval
MAFLD	Metabolic-associated fatty liver disease
SCH	Subclinical hypothyroidism
TSH	Thyroid-stimulating hormone
VDR	Vitamin D receptor
HOMA-IR	Homeostasis Model Assessment-Estimated Insulin Resistance

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

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Not applicable.

Author contributions
ZL and XL1 designed the project and developed the study protocol. ZL and XL1 conducted the literature search and collected relevant data from identified studies. ZL sorted the data and performed the initial data extraction, while SL and YF reviewed the extracted data for accuracy and completeness. ZL completed the first draft of the manuscript, while ZL, XL2, and JL were responsible for revising the draft based on feedback from co-authors. SL and YZ conducted a thorough review of the full text to ensure clarity and coherence. Additionally, SL provided financial support for the research. All authors contributed to the article and approved the submitted version.

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

Declarations

Ethics approval and consent to participate
Systematic review registration: https://www.crd.york.ac.uk/prospero/, identifier CRD42024513774.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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