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Correlation between Vitamin D levels and HbA1c in patients with Type 2 Diabetes mellitus: Systematic review with Meta-Analysis

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Abstract:

This review synthesizes findings from 21 studies conducted over 11 years to investigate the correlation between vitamin D levels and HbA1c in individuals with type 2 diabetes mellitus in India. Searches were conducted across multiple databases and included studies from 2012 to 2022. A total of 926 participants (387 females, 539 males) were included in the analysis. The majority of studies (18 out of 21) reported a mild negative correlation between vitamin D levels and HbA1c, while three studies indicated a mild positive correlation. A meta-analysis revealed a statistically significant overall pooled relationship (pooled r = -0.16, p = 0.005, 95% CI: -0.28 to -0.05), indicating that higher vitamin D levels are associated with lower HbA1c levels. These findings suggest a potential role for vitamin D in the management of type 2 diabetes mellitus, highlighting the importance of monitoring and adjusting vitamin D levels in diabetic patients. The study underscores the need for further research to elucidate the underlying mechanisms and to explore potential therapeutic implications. This review contributes to the understanding of the relationship between vitamin D and HbA1c in the context of diabetes management.

PROSPERO registration number: CRD42023404374.

Keywords:

Correlation, Vitamin D levels, type 2 diabetes mellitus, systematic review, meta-analysis

Introduction:

Diabetes is a growing health concern in India, with over half the population at risk of developing the condition at some point in their lives. [1] Hyperglycemia is a prevalent endocrine condition known as Type 2 Diabetes Mellitus (T2DM).[2] In India, the overall weighted prevalence of diabetes by oral glucose tolerance test (OGTT) was 11·4%, by HbA1c was 13.3% and it is highest when using a combination of OGTT and HbA1c is 21.1% [3]

It is still thought to be difficult to achieve normoglycemia, or ideal glucose control, even with the advancements in diabetes diagnosis and treatment. [4] This is due to the fact that treating type 2 diabetes requires strict lifestyle modifications, many prescriptions, and insulin-focused regimens. The use of traditional oral anti-diabetic drugs is linked to hypoglycemia. [5]

Since anti-diabetic medications and insulin analogs are costly, many patients in developing countries are unable to afford these prescriptions. Additionally, insulin therapy has been connected to weight gain, poor compliance, and potentially harmful cardiovascular effects. [5]

There is currently no cure for type 2 diabetes, despite constant study into long-term safety. Treatment adherence is only about 60% in spite of extensive behavioral interventions and educational initiatives. [6]

Owing to the numerous obstacles associated with diabetes care, scientists have been investigating the part that modifiable factors play in controlling type 2 diabetes. [7] A variety of factors, including as genetics, lifestyle, environment, and diet, appear to have an impact on its development. Vitamin D levels are probably one of the most important nutritional elements, either in glycemic management or in reducing the consequences of diabetes. [8-10] Worldwide recognition of vitamin D inadequacy and insufficiency is growing. [11] Furthermore, it has been connected to insulin resistance and metabolic syndrome in plasma as well as mortality in the general population. [12-13]

Epidemiological studies have linked low serum 25(OH) vitamin D levels to glucose intolerance; nevertheless, the outcomes of vitamin D-based intervention trials have been inconsistent. [15–14] Additionally, epidemiological evidence points to a potential connection between low vitamin D levels and diabetic sequelae such as neuropathy, retinopathy, and nephropathy.[14] Vitamin D levels have been shown to have a protective impact against the onset

of diabetes based on recent observational data.[16] In 2012, a meta-analysis comprising of longitudinal studies and randomised controlled trials (RCTs) came to the conclusion that there is not enough evidence to support the recommendation of vitamin D supplementation to improve insulin resistance or glycemia in patients with diabetes, normal fasting glucose, or impaired glucose tolerance.[17]

The study by Vacek et al. (2012), [18] found an important role of vitamin D levels in cardiovascular health and Diabetes and found that vitamin D level deficiency was related to reduce survival. However, the role of vitamin D levels in T2DM remains unexplored, because very few studies have explored the role of vitamin D levels and T2DM in India. [19] Long-term studies were lacking. Clinical research revealed that, even after controlling for T2DM risk variables such obesity, hypertension, and fasting glucose, there was still an inverse relationship between baseline blood vitamin D levels and incident diabetes. According to a study, during the 10-year follow-up, the concentration of vitamin D in recruited individuals was inversely correlated with their risk of developing metabolic syndrome, insulin resistance, and glucose intolerance. [20-21] Vitamin D deficiency has been linked to a higher incidence of type 2 diabetes as well as decreased insulin production and secretion. [22] The effects of vitamin D on the extra skeletal system and chronic illnesses, however, have been inconsistently demonstrated in a small number of investigations. [23-24] After the effects of insulin secretion, sensitivity, and general adiposity, there is a great deal of debate over the role that vitamin D levels play in the risk of diabetes. [25] Numerous cross-sectional studies found a negative connection between HbA1c and, [26–31] however others of the same research found a little positive correlation. [32–34] There was a negative connection between HbA1c and other cross-sectional analytical investigations. [35]

Those studies which have done a comparison with non-diabetic subjects also showed an inverse correlation with HbA1c among diabetics. As a result, research conducted over the past 10 years has produced contradictory findings about the relationship among vitamin D levels with the diabetes test HbA1c. The purpose of the current study was to determine whether vitamin D levels and HbA1C in patients with Type 2 Diabetes are related.

Materials and Methods:

Search strategy:

The following meta-analysis and systemic review followed the Preferred Reporting

Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) standards.[36] The study was registered to PROSPERO (CRD42023404374).

In the present analysis using cross-sectional data from 2012 to 2022 to evaluate whether vitamin D levels are correlated with HbA1c in individuals with diabetes. A comprehensive statistical analysis of the relationship between vitamin D levels and HbA1c in type 2 diabetic was achieved through a systematic review and meta-analysis of health science papers.

The electronic databases were thoroughly searched, including “BMC, BMJ, Science Direct, Scopus, PubMed, Embase, Sage, and Taylor and Francis were systematically searched, using the keywords “India” AND “Vitamin D levels” OR “25(OH) Vitamin D” OR “25(OH) D” AND “HbA1c” OR “Glycated Hemoglobin” AND “Correlation” OR “Association” AND “Type 2 Diabetes” OR “T2DM”. Furthermore, studies that were "hand searched" were also manually searched.

Inclusion and Exclusion Criteria:

The inclusion criteria were: 1. Research in the health sciences demonstrating the relationship between vitamin D levels and HbA1c. 2. First-hand, English-language, peer-reviewed Indian Studies 3. Research works released from 2012 to 2022.

The exclusion criteria were: 1. Excluded research included case reports, review articles, book chapters, and conference abstracts. 2. Research that did not provide the precise correlation coefficient was eliminated. 3. Interest correlation between pregnancy, 4. The correlation coefficient between patients with vitamin D insufficiency, Studies where the correlation value (r) was mentioned after classifying vitamin D and HbA1c, as opposed to studies that just reported the type of correlation.

Data Extraction and Quality Assessment:

Two independent reviews were given to the eligible papers to extract the correlation coefficients, study design, sample size, year, author, and article title. Duplicate articles were eliminated when possibly eligible articles were identified. With the help of a third reviewer, disagreements over what should be included or excluded were settled. The author of the paper was contacted via email if any of the studies did not provide pertinent information. For cross-sectional observational and

case-control studies, the Newcasle-Otawwa Quality Assessment Scales were used to assess the studies' quality. [37] (Table x OTAWWA)

By utilising Fisher's z transformation of correlations, effect sizes were computed. To convert r to a z-score, use the formula $z' = 0.5[\ln(1+r) - \ln(1-r)]$. if there was statistical heterogeneity ($p<0.05$, $I2 >50\%$). [38] If not, the data were pooled and analysed using the random-effects model (limited maximum-likelihood estimator) after being adapted to the fixed-effects model (method: inverse-variance). Since heterogeneity was discovered in the current investigation, the random effect model was applied. The present study evaluates the publishing bias using a funnel plot. A popular diagnostic plot in meta-analyses is the funnel plot, which is particularly useful for evaluating publication bias and small-study effects. [39]

Data Analysis:

Meta-analysis was carried out by JASP 0.16.3.0 Software. Effect size and standard error were calculated using David Wilson's "Meta-analysis effect size calculator".[40] To measure the publication bias, the Funnel plot's Rank correlation test was utilised.

The association between moderators and effect magnitude was examined by the random forest model. The Rank-test was used to quantitatively analyse the asymmetry of the funnel plot.

Results:

Studies used different databases, the most commonly used sources were PubMed, Scopus, BMJ, Science Direct, Sage, BMC, and Trailar and Francies. The total number of studies included from these different sources was 224. Furthermore, 110 hand-search articles were included in the present study. The survey comprised 334 publications in total from several health areas. There were 4601 participants overall from 334 articles. Finally, after screening, 21 studies met the eligibility criteria. (Figure1)

Table 1 Characteristics of the included studies and year, sample size, technique used, and gender of participants. The correlation coefficient of the vitamin D level with HbA1c in diabetes patients is shown. Six comparative, ten cross-sectional, and one retrospective study were discovered from the selected studies.

The Study design was not mentioned in 5 studies. Only 9 studies have given data about gender. Among these total Sample sizes of males and females were 539 and 387 respectively. The total number of studies included was 21. (Table 1)

This systemic review showed that majority of the studies (18 studies) have shown negative correlation, and in 3 studies positive correlation was observed. The negative correlation coefficient ranges from -0.0046 to -0.993. One study showed a perfect negative correlation, whereas few studies showed a very mild or negligible correlation between vitamin D and HbA1c. Positive correlations ranging from 0.061 to 0.333 were seen in several studies. There was just a weak positive connection, not a significant one, between vitamin D and HbA1c. (Reference Table 1). The pooled correlation between Vitamin D and HbA1c was r=- 0.16, (95% CI is -0.28 to -0.05 (Figure 2). The heterogeneity was found high, (I^2=88.851%, P<0.005), so a random effect model was used. (Table 2, 3 & 4). Based on the total effect size estimate, the funnel plot (Figure 3) suggests that the measured effect sizes appear to be dispersed evenly along the vertical axis. Asymmetry is frequently used as a sign of publication bias. The "Rank Correlation Test" for funnel plot asymmetry is included with this plot and, in this instance, the results are non-significant (p=0.928). (Table 5).

Discussion:

The available information is insufficient to make a definitive judgement on the relationship involving vitamin D levels with HbA1c in people with Type 2 Diabetes. A review of different studies showed different conclusions like Inverse correlation, positive correlation, and negligible correlation between the same. As a result, the current systematic and meta-analysis study showed that vitamin D levels and HbA1c had a negative association. (95% CI is -0.28 to -0.05) and r=-0.16. We found enough research, based on a thorough examination of the literature and stringent inclusion and exclusion criteria, to do a meta-analysis of papers released between 2012 and 2022.

Blood vitamin D level and HbA1c had a considerable inverse relationship (r=-0.263, p=0.000465), according to studies by Ramu Adela et al. [41,42] Compared to control, T2DM, and CAD participants, vitamin D metabolites were reduced in T2DM plus CAD subjects. Vitamin D metabolites like 25(OH) D can be used to predict T2DM, while 1,25(OH)2D can be used to predict CAD in T2DM. Deep Dutta et al.'s study [42] revealed a negligible, insignificant negative connection (r=-0.07, p=0.880) between vitamin D levels and HbA1c. In our nation, prediabetes patients with a high cardiovascular risk may develop or exacerbate insulin resistance due in part to vitamin D deficiency

or insufficiency. Ahmad Hayat Bhat and others, [35] discovered a significant inverse relationship (r=-0.225, p=0.035) between vitamin D levels and HbA1c. A fairly prevalent health issue, vitamin D insufficiency is comparatively more common among T2DM patients. According to Durgaroa et al. [43], there was a very little and insignificant negative connection (r=-0.05, p=0.60) between vitamin D levels and HbA1c. Things could get worse due to the prevalence of severe vitamin D insufficiency and its independent correlation with the glycemic and lipid profiles of Type 2 diabetes. Tyagi Ankit et al. [26] revealed that there was a very small and insignificant negative connection (r=- -0.0046, p= 0.9687) between vitamin D levels and HbA1c. There was no discernible correlation found between vitamin D levels as well as type 2 diabetes. Vitamin D and HbA1c were found to be significantly unrelated.

Dr. Ayesha Juhi et al. [27] revealed a strong inverse relationship (r=-0.3, p=0.013) between vitamin D levels and HbA1c. Physiologically speaking, it would make sense to provide vitamin D supplements to those with type 2 diabetes to improve blood sugar regulation. Balasubramanian Shanthi et al [44] indicated a tendency towards a negative 25(OH)D-HbA1c connection, although this trend was not statistically significant. The correlation between the research population's higher HbA1c and low blood 25(OH)D levels may probably be interpreted in a broader light, indicating vitamin D deficiency is a poor prognostic factor that would be crucial in compromising glycaemic management. Dipesh Patel et al. [45] revealed a strong unfavorable relationship (r=-0.281, p<0.001) between vitamin D levels and HbA1c. Compared to the general healthy population, vitamin D insufficiency is far more common among diabetic patients. Serum vitamin D levels should be monitored in all type 2 diabetic patients for better management of hyperglycaemia. Take vitamin D pills as soon as a deficiency is identified. Havilah Polur et al. [46] revealed a highly significant negative connection (r=-0.993, p<0.0001) between vitamin D levels and HbA1c. This study found a negative relationship between vitamin D, future glycemia, and insulin resistance. This could help prevent type 2 diabetes and be crucial in understanding the etiology of aberrant glucose metabolism. Kirubhakaran Kanakaraju et al. [28] revealed a significant but very weak negative connection (r=-0.037p<0.001) between vitamin D levels and HbA1c. The primary approach to determining if vitamin supplementation is a helpful tactic in preventing or postponing the onset of type 2 diabetes will be studied such as randomized controlled trials. Testing for vitamin D3 levels may be helpful for people at risk of type 2 diabetes, even though it may not be required for healthy persons at this time.

The study by Mamatha Patil et al. discovered a substantial mild negative connection (r=-0.390 p<0.001) between vitamin D levels and HbA1c. [47] The study concludes that poor glycaemic control and obesity are the most frequent causes of female diabetes patients, with virtually all of them having vitamin D deficiency. Therefore, every diabetes patient needs to make life changes, start taking vitamin D supplements at an early age, and manage their blood sugar levels. Our analysis yielded a similar negative correlation result. A study by Mehta et al. found that in those with Type II diabetes, low vitamin D levels are linked to high HbA1c. The two measures, vitamin D and HbA1C, have an inverse connection (r=0.1205). Patients with diabetes may have routine veterinary vitamin D screenings. [48] Another study found a negative connection (r=-0.013, p=918) between vitamin D levels and HbA1c, which is consistent with our findings. [49]. The study concludes that while it is unclear whether vitamin D supplementation helps glycemic status, higher vitamin D levels may contribute to improving people's general health. The results of the current investigation are corroborated by the research conducted by Sunusi Usman Maaji et al. [50]. The main finding of the study is that there is a negative connection (r=-0.109) between HbA1c and vitamin D status, indicating that HbA1c levels decrease with increasing vitamin D levels. That was his recommendation. The association between these two indicators may be explained by the influence of vitamin D on the pancreatic β-cell, which improves glucose homeostasis and insulin action. Alternatively, vitamin D may modify hemoglobin. Additionally, a study discovered a strong inverse relationship (r=-0.329, p=0.001) between blood levels of 25(OH) D and HbA1c. According to the study's findings, patients with vitamin D deficiency had higher HbA1c values. Maintaining dyslipidemia and 25-hydroxyvitamin D levels is crucial for improved control of HbA1c levels in those with Type 2 Diabetes mellitus. [51]

After researching the relationship between vitamin D and HbA1c levels in individuals with Type 2 Diabetes mellitus, Suguna et al. [29] concluded that there isn't a statistically significant association between the two (r=-0.109, p=0.568). The results obtained from this investigation have similarities to those of studies conducted by Samiramiss Ghavan et al and Gauhar Nadri et al [30–31]. The results of the Pearson's correlation test indicated that the levels of vitamin D and HbA1c had a negative linear link (r=-0.088, p=0.378 and r=-0.38, p<0.0001). Due to the interaction between vitamin D levels and insulin action, the study concludes that it looks beneficial to monitor vitamin D blood levels in diabetes patients and, if necessary, offer supplements.

To determine whether 25-hydroxyvitamin D (25OHD) has a clinically significant impact on hemoglobin glycation (HbA1c) and insulin resistance in T2DM subjects, a comparative study between T2DM cases and non-diabetic controls was conducted by Jayesh J Sheth et al. [33]. The results of the study indicated a weakly positive connection (r=0.33) between HbA1c and vitamin D levels. This study found that although vitamin D deficiency is common in people with type 2 diabetes, there is insufficient evidence to link it to insulin resistance or glycation control in T2DM patients. It suggests that while improved health outcomes can be attributed to greater vitamin D status, dietary and lifestyle adjustments also seem to have a significant role. The purpose of the study by C. Akash et al. [34] was to determine the relationship between TL and Vitamin D in T2DM as well as the effect of Vitamin D on TL in patients with T2DM. The findings revealed a weak and statistically insignificant relationship (r=0.08 p=0.0.5897) between vitamin D levels and HbA1c. This result is corroborated by a study done by Riyaz Ahmad Daga et al. [52]. It made an effort to assess the juvenile diabetics' vitamin D status. The study found that, in comparison to controls, individuals with diabetes had considerably lower mean levels of vitamin D. Furthermore, the study found no connection between vitamin D levels and HbA1c.

This is the first thorough national meta-analysis that, to the best of our knowledge, explains the connection between vitamin D levels and HbA1c in India. This study's strength is precisely this. Overall, there was a statistically significant connection (r=-0.16, p = 0.005, 95% CI: - 0.28 to -0.05) between the vitamin D level and Hba1c. With the same goals, Ali Shlash Al-Ibrahimy et al. did a similar review and meta-analysis study that produced a similar result (p = 0.001, 95% CI: -0.230 to -3.268). [53]

It is plausible that vitamin D levels have an impact on the pathophysiology of type 2 diabetes given the inverse association shown between HbA1c and vitamin D levels. Consequently, vitamin D correction benefits diabetics who have low blood sugar. Thus, further studies are needed to demonstrate the possible advantages of vitamin D supplementation and status adjustments for glycemic index correction.

Contributors:

V.M. and M.M. conceptualized the study and designed the protocol Together, they led the data visualization, conducted article searches, evaluated the literature, and penned the first draft. The reviews and editing were written by the same authors. V.M., M.M., R.U., M, and R.S.D. authorized the final copy for publishing and added to its intellectual content. Each author assumed responsibility for the accuracy and integrity of the content and had complete access to the study's data.

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Abbreviations:

1. Vit. D: Vitamin D
2. Hba1c: Glycosylated hemoglobin
3. T2DM: Type2- diabetic
4. LDL: low-density lipoprotein
5. TG: Triglyceride

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TABLES AND FIGURES:

Table 1: Characteristics of 23 included studies. Correlation between Vitamin D levels and HbA1c; Correlation coefficient with significant value: Sample size; Study design

S.NO	AUTHOR	YEAR OF PUBLISH	CORRELATION	Effect size	p value	Study design	SAMPLE SIZE	FEMALE	Male
1	Ramu Adela et al.	November-2016	-0.263	-0.263	0.0004	Comparative study	187	61	126
2	Jayesh J Sheth1 et al.	February-2015	0.333	0.333	0.045	cross sectional study	429	-	-
3	C. Akash1 et al.	November-2021	0.08	0.08	0.5897	Cross sectional study	90	27	18
4	Deep Dutta et al.	December-2013	-0.07	-0.07	0.88	Not mentioned	157	-	-
5	Mohammad Hayat Bhat et al.	December-2020	-0.225	-0.225	0.035*	Cross-sectional analytical	108	53	55
6	Durgaroa et al.	January-2017	-0.05	-0.05	0.6	Case control study	200	-	-

7	Ankit Tyagi et al.	December-2019	-0.0046	-0.0046	0.9678	Cross sectional study	100	-	-
8	Dr.Aysha Juhi et al.	2019	-0.3	-0.3	0.013	Cross sectional study	63	-	-
9	Balasubramanian Shanthi et al.	June-2012	-0.173	-0.173	0.229	Not mentioned	50	-	-
10	Dipesh Patel et al.	June-2020	-0.281	-0.281	<0.001	Case-control study	70	82	58
11	Havilah polur et al.	2013	-0.993	-0.993	<0.001	Case control study	120	-	-
12	Kirubhakaran Kanakaraju et al.	May-2017	-0.037	-0.037	0.001	Cross sectional study	100	50	50
13	Mamatha Patil et al.	December-2018	-0.39	-0.39	<0.001	Not mentioned	156	156	0
14	Niyati Mehta et al.	June-2016	-0.12	-0.12	not mentioned	Not mentioned	100	-	-

15	P Santosh kumar et al.	June-2022	-0.013	-0.013	0.912	Not mentioned	80	-	-
16	RIYAZ Ahmad daga et al.	August-2012	0.061	0.061	not mentioned	Case control study	72	-	-
17	Sunsi Usman et al.	June-2014	-0.109	-0.109	0.030317	Retrospective Cohort Study	395	-	-
18	Suman Lata et al.	June-2021	-0.329	-0.329	0.001	Discriptive Case Control Study	200	-	-
19	Suguna S et al.	December-2019	-0.109	-0.109	0.568	Cross-Sectional	50	-	-
20	Samiramiss Ghavam et al.	December-2018	-0.088	-0.088	0.378	Cross-Sectional descriptive	102	74	28
21	Gauhar Nadri et al.	April-2021	-0.38	-0.38	<0.001	Cross sectional	88	36	52
Total							2917	539	387

Table 1a: Quality assessment of included studies

Observational, cohort and cross sectional studies															
SN	**AUTHOR NAME**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**
1	Joao SoaresFelicio et al.	YES	YES	YES	YES	NO	YES	NO	OTHERS	YES	OTHERS	YES	OTHERS	OTHERS	NO
2	Dr Ayesha Juhi	YES	YES	YES	YES	NO	OTHERS	OTHERS	OTHERS	YES	OTHERS	YES	OTHERS	OTHERS	NO
3	Balasubramanian shanthi	YES	YES	YES	YES	NO	OTHERS	OTHERS	OTHERS	YES	OTHERS	YES	OTHERS	OTHERS	NO
4	Kirubhakaran Kanakaraju	YES	YES	YES	YES	NO	OTHERS	OTHERS	OTHERS	YES	OTHERS	YES	OTHERS	OTHERS	NO
5	MAMATHA B PATIL	YES	YES	YES	YES	NO	OTHERS	OTHERS	OTHERS	YES	OTHERS	YES	OTHERS	OTHERS	NO
6	Niyati Mehta	YES	YES	YES	YES	NO	OTHERS	OTHERS	OTHERS	YES	OTHERS	YES	OTHERS	OTHERS	NO
7	P. Santosh Kumar	YES	YES	YES	YES	NO	OTHERS	OTHERS	OTHERS	YES	OTHERS	YES	OTHERS	OTHERS	NO

8	Samiramiss Ghavam	YES	YES	YES	YES	YES	OTHERS	OHERS	OTHERS	YES	OTHERS	YES	OTHERS	OTHERS	NO
9	Suguna S	YES	YES	YES	YES	YES	OTHERS	OTHERS	OTHERS	YES	OTHERS	YES	OTHERS	OTHERS	NO
10	Sunusi Usman Maaji	YES	YES	YES	YES	NO	OTHERS	OTHERS	OTHERS	YES	OTHERS	YES	OTHERS	OTHERS	NO
CASE CONTROL STUDIES															
SN	**AUTHOR NAME**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**		
1	Ankit Tyagi	YES	YES	NO	YES	YES	YES	NO	YES	NO	OTHERS	OTHERS	NO		
2	Gauhar Nadri	YES	YES	YES	YES	YES	YES	NO	YES	NO	OTHERS	OTHERS	YES		
3	Dipesh Patel	YES	YES	NO	YES	YES	YES	NO	YES	NO	NO	NO	NO		
4	Havilah Polur	YES	YES	NO	YES	YES	YES	NO	YES	NO	NO	NO	NO		

5	Durgarao Y	YES	YES	NO	YES	YES	YES	NO	YES	NO	NO	NO	NO		
6	RAMU ADELA	YES	NO	NO	YES	NO	YES	NO	YES	NO	NO	NO	YES		
7	Mohammad Hayat Bhat	YES	YES	NO	YES	YES	YES	NO	YES	NO	NO	NO	NO		
8	Riyaz Ahmad Daga	YES	YES	NO	YES	YES	YES	NO	YES	YES	YES	NO	NO		
9	Suman Lata	YES	YES	NO	YES	YES	YES	YES	YES	NO	YES	NO	YES		
10	C. AKASH	YES	YES	YES	YES	YES	YES	NO	YES	NO	NO	NO	YES		
11	Jayesh J Sheth	YES	YES	YES	YES	YES	YES	NO	YES	NO	YES	NO	NO		
12	Deep Dutta	YES	YES	YES	YES	YES	YES	NO	YES	YES	NO	NO	NO		

Table 2 : **Fixed and Random Effects**

Fixed and Random Effects

	Q	df	p
Omnibus test of Model Coefficients	8.008	1	0.005
Test of Residual Heterogeneity	220.615	20	< .001

Note. *p* -values are approximate.

Note. The model was estimated using Restricted ML method.

Table 3 : **Coefficients**

	Estimate	Standard Error	z	p
intercept	-0.164	0.058	-2.830	0.005

Note. Wald test.

Table 4 : **Residual Heterogeneity Estimates**

	Estimate
τ^2	0.060
τ	0.245
I^2 (%)	88.851
H^2	8.969

Table 5: Rank correlation test for Funnel plot asymmetry

	Kendall's τ	p
Rank test	0.014	0.928

Figure 1: Flow chart of selection of studies

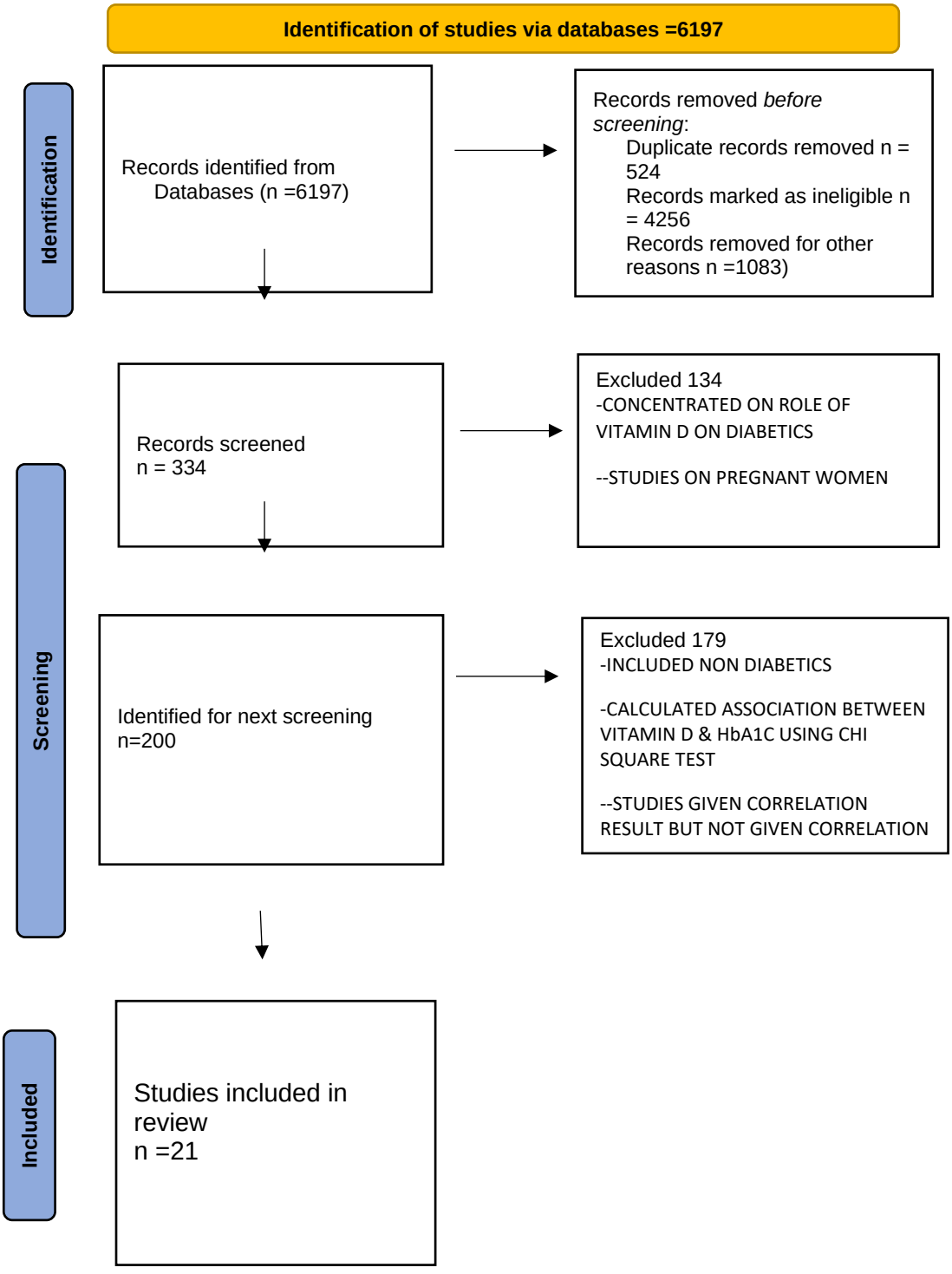

Figure 2: Forest Plot

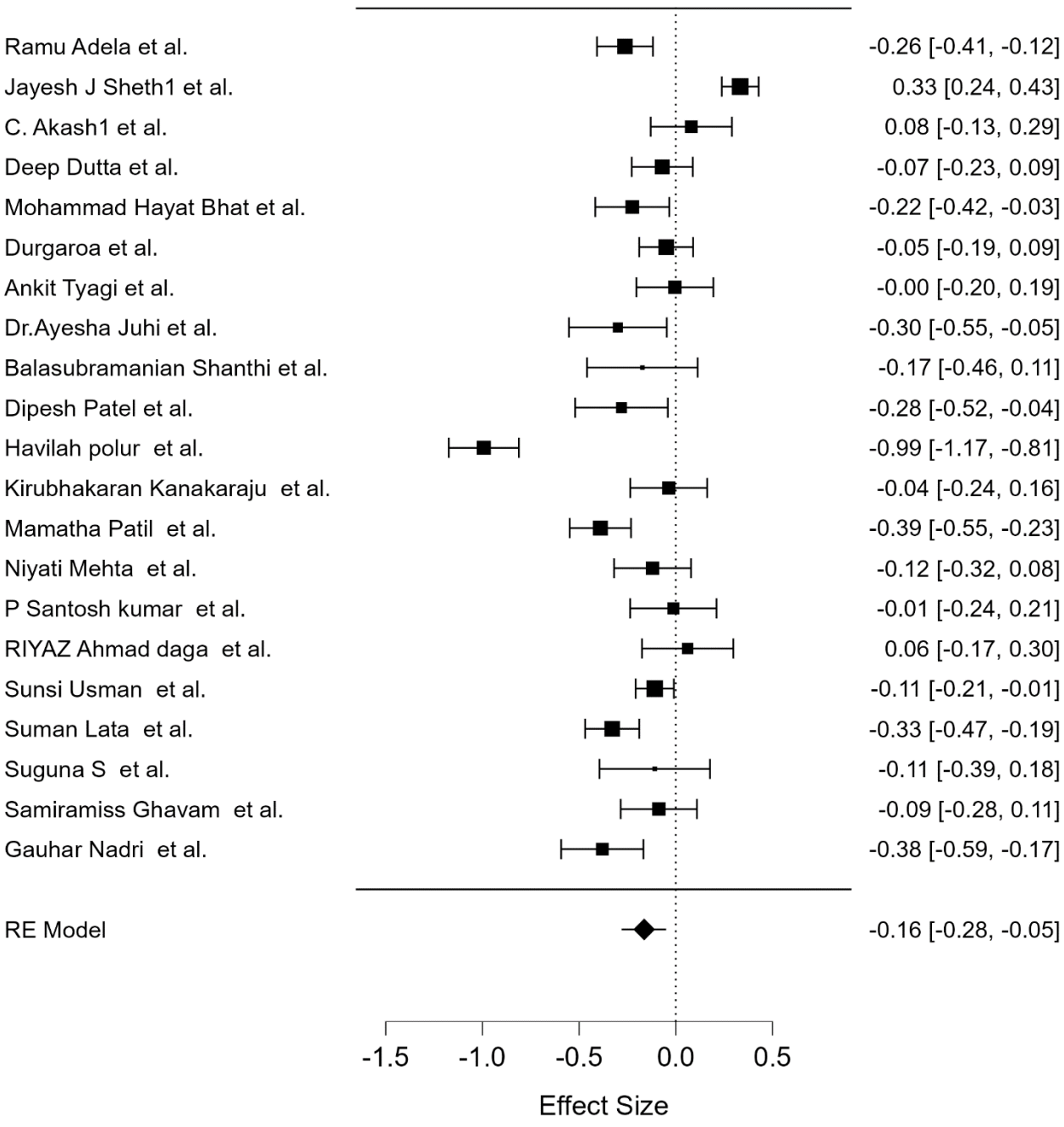

Figure 3: Funnel Plot