



Effect of low glycemic index diet on HbA1c in type 2 diabetes mellitus: A systematic review and meta-analysis in Asia

Pengaruh diet indeks glikemik rendah terhadap HbA1c pada penyandang diabetes melitus tipe 2: Systematic review dan meta-analysis di Asia

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Abstract

Diabetes mellitus affects 10.5% of the global population, and its prevalence is expected to increase by 2045. Type 2 diabetes mellitus (T2DM) is commonly associated with abnormal HbA1c levels, lipid metabolism, and body mass index (BMI). A low glycemic index (GI) has been proposed to improve HbA1c, lipid profiles, and BMI, but the findings remain inconsistent, and most studies have been conducted in non-Asian populations. This study evaluated the effect of a low-GI diet on HbA1c levels in Asian adults with T2DM. Systematic searches in the PubMed, ScienceDirect, and Scopus databases identified randomized controlled trials (2014-2024) involving adults (≥ 18 years) with T2DM, excluding pregnant and breastfeeding women. Meta-analysis and subgroup analysis were conducted, and meta-regression was used to assess the moderators. Study quality was assessed using the ROB-2 and GRADE. Of the 1,485 articles screened, 16 met the inclusion criteria. The low-GI diet significantly reduced HbA1c and LDL levels and increased HDL levels. Subgroup analysis showed variations between the intervention and control groups, with the percentage of female participants and supplementation type as potential moderators. Despite statistical significance, the small effect size, heterogeneity, and low-to-moderate certainty of evidence (GRADE) suggest limited clinical relevance. Further research should consider the sample size, female proportion, and type of intervention in the control group to strengthen the evidence for clinical and policy applications.

Keywords: Asia, dietary intervention, glycemic index, type 2 diabetes, systematic review.

Abstrak

Diabetes mellitus mempengaruhi 10,5% populasi global, dengan prevalensi yang diperkirakan akan meningkat pada tahun 2045. Diabetes melitus tipe 2 (T2DM) sering dikaitkan dengan kadar HbA1c, profil lipid, dan indeks massa tubuh (BMI) yang abnormal. Indeks glikemik (GI) rendah telah diusulkan dapat membantu memperbaiki HbA1c, profil lipid, dan BMI, namun temuan masih inkonsisten, dan sebagian besar studi dilakukan pada populasi non-Asia. Penelitian ini mengevaluasi efek diet GI Rendah terhadap HbA1c pada dewasa T2DM di Asia. Pencarian sistematis melalui database PubMed, ScienceDirect, dan Scopus untuk mengidentifikasi *randomized controlled trial* (2014-2024) yang melibatkan dewasa (≥ 18 tahun) dengan T2DM, kecuali wanita hamil dan menyusui. Meta-analisis dan analisis subgroup dilakukan, dengan meta-regresi untuk menilai moderator. Kualitas studi dinilai menggunakan ROB-2 dan GRADE. Dari 1.485 artikel terskrining, 16 artikel memenuhi kriteria inklusi. Diet GI rendah secara signifikan menurunkan HbA1c dan

LDL, serta meningkatkan HDL. Analisis subgroup menunjukkan variasi antara kelompok intervensi dan kontrol dengan persentase peserta perempuan dan tipe suplementasi diidentifikasi sebagai moderator. Meskipun signifikan secara statistik, efek yang kecil, heterogenitas, dan bukti kepastian Rendah-sedang (GRADE) menunjukkan relevansi klinis yang terbatas. Penelitian lebih lanjut perlu mempertimbangkan besar sampel, proporsi perempuan, dan jenis intervensi pada kelompok kontrol supaya memperkuat bukti untuk aplikasi klinis dan kebijakan.

Kata Kunci: Asia, intervensi diet, indeks glikemik, diabetes tipe 2, *systematic review*.

Introduction

Diabetes Mellitus is a global health problem with a prevalence of 10.5% in 2021, and it is predicted to increase to 12.2% by 2045, with type 2 diabetes mellitus (T2DM) accounting for more than 90% of diabetes cases worldwide (International Diabetes Federation, 2021). It is estimated that 94% of the increase in the number of people with diabetes by 2045 will occur in low- and middle-income countries, where population growth is expected to be greater, and Asian countries fall into that category (International Diabetes Federation, 2021).

The American Diabetes Association (2014) recommends glycated hemoglobin (HbA1c) instead of fasting blood glucose to diagnose diabetes (American Diabetes Association (ADA), 2014). HbA1c can be a good predictor of lipid profiles and thus can be used for people with DM who are at risk of cardiovascular complications. Maintaining HbA1c levels <7% for 5 years is associated with a reduced rate of diabetes-related complications compared with maintaining HbA1c > levels >7% (Boye et al., 2022).

Dietary modification aimed at implementing a healthy diet that can improve glycemic control is an important component of T2DM management. There is no consensus on the ideal nutritional strategy and percentage of calories, carbohydrates, proteins, and fats in patients with T2DM. Thus, the type of strategy and macronutrient distribution should be based on an individualized assessment of the current diet, preferences, and metabolic goals of the individual. To date, the list of food glycemic indices (GI) and glycemic loads (GL) has become a guideline for people with DM in choosing the type of food consumed to control blood sugar levels (Mulyo et al., 2022). The glycemic index

(GI) is an index of carbohydrate foods that indicates how quickly or slowly these nutrients can cause an increase in blood glucose, which is a number from 1 to 100, with 100 representing pure glucose (Jenkins et al., 1981 in Penlioglou et al., 2021). Foods are categorized as having low GI (≤ 55), medium GI 56-69, and high GI (≥ 70) (Brand-Miller & Buyken, 2020). Factors affecting GI include food fiber, amylose, and amylopectin content, fat and protein content, and processing methods (Arif et al., 2014).

A low-GI diet has many benefits for people with T2DM; however, contradictory results have been reported. The implementation of a high-GI diet (GI = 63), low-GI diet (GI = 55), and low-carbohydrate diet (GI = 59) in individuals with T2DM did not affect long-term HbA1c levels (Wolever et al., 2008). In contrast, the results of the meta-analysis and sensitivity test showed a significant difference ($p < 0.001$ and $p < 0.001$, respectively) between the low-GI and high-GI or control diets in HbA1c levels (Ojo et al., 2018). A study conducted by Zafar et al. (2019) reported that a low-GI diet was effective in reducing glycated hemoglobin (HbA1c), fasting glucose, body mass index (BMI), total cholesterol, and LDL, but did not affect fasting insulin, HOMA-IR, HDL, triglycerides, or insulin requirements. Research methods, such as controlled trials and reviews, have yielded varying results.

Research on low-GI diets in patients with T2DM has been conducted on non-Asian populations; therefore, the generalization of the results to Asian populations is still limited. In addition, several studies have measured parameters such as HbA1c or lipid profiles separately, but the effects of low-GI diets on HbA1c, lipid profiles, and body mass index have not been comprehensively explained. We conducted a systematic review and meta-analysis of the effects of a low GI diet on HbA1c in Asia.

Methods

This systematic review and meta-analysis was conducted following the Cochrane 2020 PRISMA guidelines. Searches were conducted in three databases: PubMed, ScienceDirect, and Scopus. The inclusion criteria for this study were as follows: research publications in English from the last 10 years (2014-2024), research involving individuals with T2DM aged ≥ 18 years, interventions provided in the form of a low-GI diet (supplementation, whole food, combination with nutrition counseling), location in Asia, and RCT research design.

Food supplementation involves adding low-GI foods to the diet of individuals with DM2. Food supplements may contain carbohydrates, such as fiber. These supplements are available in various forms, such as tablets, capsules, powders, liquids, and easily dissolvable tablets (Institute for Quality and Efficiency in Health Care (IQWiG), n.d.). Low-GI foods have a glycemic index value of ≤ 55 , which, when consumed, results in a low blood glucose response (Brand-Miller & Buyken, 2020). Nutrition counseling is the provision of education, understanding, and training regarding knowledge and skills in diabetes management given to every person with diabetes to address their issues (Akerina et al., 2023).

Pregnant and breastfeeding women were excluded from the study. In normal, non-diabetic pregnant women, HbA1c levels decrease during the second trimester of pregnancy and increase in the third trimester (Rawal et al., 2016). This indicates a unique characteristic in pregnant women.

Search terms used synonyms, Medical Subject Headings (MeSH), and Boolean operators (AND/OR) to combine the words. The primary outcome was HbA1c (%), and the secondary outcomes were high-density lipoprotein (HDL) (mg/dL), low-density lipoprotein (LDL) (mg/dL), triglycerides (mg/dL), and body mass index (kg/m^2). The external variables were age (years), percentage of females (%), duration of interventions (weeks), type of comparison/control, and study quality.

Categorization of outcomes based on changes from the baseline, as reported in the study. Intervention types were categorized as supplementation, supplementation and nutrition counseling, and food. The comparison/control

groups were those that did not receive the main intervention. The intervention duration was categorized as <8 , $8-12$, and >12 weeks. Study quality was assessed using the ROB-2 tool, which was evaluated based on five domains and categorized as good, moderate, or poor (Higgins et al., 2023).

Intervention is provided in the form of a low glycemic index (GI) diet; a diet with certain food ingredients that are matched with food tables with $\text{GI} < 55$; a diet that is indirectly similar to a low GI diet, such as providing food products that have high total dietary fiber content, amylose/amylopectin content, and fat and protein content (Arif et al., 2014). Examples of food ingredients with a low GI include psyllium, chia seeds, almonds, brown rice, oats, pistachios, tartary buckwheat, flaxseed, jackfruit flour, and red dates. The comparator group followed a low-GI diet, low-GI whole meal, or a combination of a low-GI diet with nutritional advice/physical activity/specific medication.

Screening was conducted for each database, and duplicates were excluded. Articles were screened based on their titles and abstracts, and the full texts were independently reviewed by two reviewers with the help of the Rayyan AI application. The results were reported using a PRISMA flow chart. A third independent reviewer will be involved in the event of any disagreement between the two reviewers. Risk of bias assessment in the study was independently conducted by two reviewers using The Risk of Bias 2 (ROB-2) tool for Randomized Controlled Trial (RCT) studies (Higgins JPT et al., 2023).

Synthesis in the form of SMD is presented with a confidence interval (95%CI) and a prediction interval (PI). The prediction interval (PI) is used to examine the distribution of the true effect size and error. Meta-analysis and meta-regression were performed using RevMan 5.2 and RStudio 4.2.2. Cochrane's Q test value < 0.10 and I^2 value $\geq 30\%$ were considered to indicate heterogeneity (Deeks et al., 2023). Subgroup analyses included the duration of intervention, type of intervention, comparison/control group, and the quality of the study.

The publication bias of the included studies was subjected to meta-bias analysis using Egger's test with p -value < 0.05 , considered as publication bias, and presented by a funnel plot. Each RCT was plotted in a simple scatter

plot according to the intervention effect and standard error of the effect estimates. Funnel plots were created using RevMan 5.2 and RStudio 4.2.2 software. Any asymmetry or anomaly in the funnel plot has been reported previously (Higgins JPT et al., 2023).

Publication bias from the included studies was analyzed by meta bias using Egger's test, with a p-value <0.05 considered as publication bias and presented with a funnel plot. Funnel plots were created using RevMan 5.2 and RStudio 4.2.2 (Higgins JPT et al., 2023). Evidence analysis was performed using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) tool. GRADE is a system for assessing the quality of evidence for each outcome in a review based on eight criteria. The quality of evidence was rated as high, moderate, low, or very low, reflecting the level of confidence in the impact estimate. High-quality evidence indicates a strong confidence in the estimate (Ryan & Hill, 2016).

This study was approved by the Ethics Commission of the Faculty of Medicine, Public Health, and Nursing, University of Gadjah Mada (number KE/FK/0590/EC/2024) on April 22, 2024, and was registered in the PROSPERO International prospective register of systematic reviews on April 10, 2024.

Result and Discussion

Selection Study Characteristics, and Research Quality

The results of the identification of 1485 articles from three databases and 16 articles that met the inclusion criteria were then subjected to a systematic review and meta-analysis. Five studies were conducted in Iran (32%), four in China (25%), two in India (13%), one in Palestine (6%), one in Kuwait (6%), one in Thailand (6%), one in Taiwan (6%), and one in Japan (6%). All the included studies were published between 2014-2024. The study design included a 100% Randomized Controlled Trial (RCT). People with type 2 diabetes mellitus (T2DM) are aged 18–80 years. Five studies were conducted in clinics (31%), 10 in hospitals (63%), and one in a diabetes research center (6%). Data scraping was performed on studies with varying interventions, durations, and

comparators/controls so that the outcomes had different numbers of studies and participants. Five studies had a low risk of bias (31%), eight had a moderate risk of bias (50%), and three had a high risk of bias (19%).

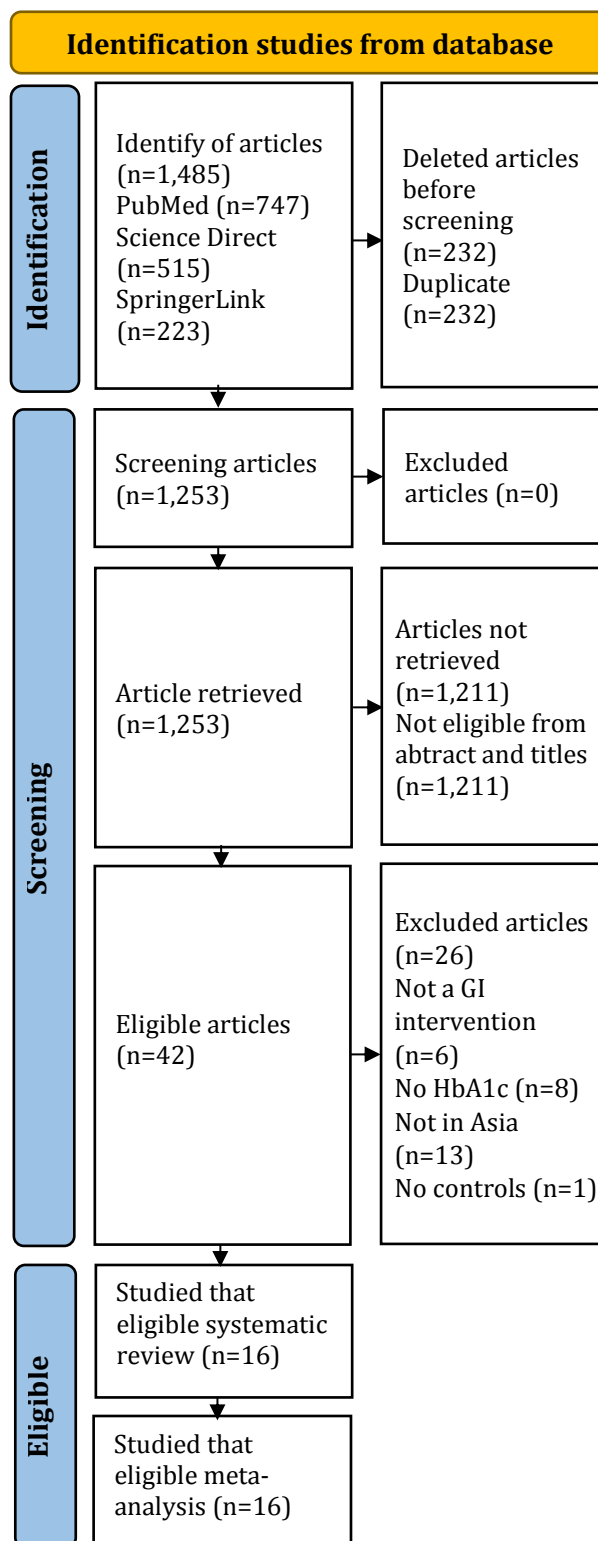


Figure 1. PRISMA diagram

Meta-Analysis Results

The effect of low GI on HbA1c had a significantly decreased SMD of -0.38 with a 95%CI estimate range [-0.51 to -0.25]. The distribution of the effect size of low GI on actual HbA1c was within the PI estimate range [-0.81, 0.05]. This outcome showed I² heterogeneity (45%). The effect of low GI on HDL had an SMD increase of 0.14 with a 95%CI estimate range [0.02–0.26]. The distribution of the effect size of low GI on actual HDL levels was within the PI estimate range [-0.20; 0.48]. This outcome indicated I² heterogeneity (32%).

The effect of low GI on LDL had a significantly decreased SMD of -0.30 with a 95%CI estimate range of [-0.40, -0.20]. The actual distribution of the effect size of low GI on LDL was within the PI estimate range [-0.41, -

0.19]. The outcome showed no I² heterogeneity (0%). The effect of low GI on triglycerides had an insignificant increase in SMD of 0.02, with an estimated range of 95%CI [-0.12; 0.17]. The distribution of the effect size of low GI on actual triglyceride levels was within the PI estimate range [-0.46; 0.51]. This outcome showed I² heterogeneity (48%).

The effect of low GI on BMI had a decrease in SMD of -0.04 with an estimated range of 95%CI [-0.15; 0.08] that was not significant. The distribution of the effect size of low GI on actual BMI was within the PI estimate range [-0.16, 0.09]. This outcome had no heterogeneity I² (0%) or fixed-effect model. This outcome was associated with publication bias. After trim and fill, low GI increased BMI with SMD of 0.02 kg/m² with 95%CI estimate range [-0.08; 0.13], I² = 0%.

Table 1. Results of meta-analysis of the effect of low glycemic index diet on HbA1c, HDL, LDL, triglycerides, and BMI

Outcome	Individuals with type 2 diabetes mellitus (T2DM)				
	N	Std. Mean Difference (95% CI)	Prediction Interval (PI)	Cochrane's Q test	I ² %
HbA1c (%)	24	-0.38 [-0.51; -0.25]*	-0.81; 0.05	0.01	45
HDL (mg/dL)	20	0.14 [0.02; 0.26]*	-0.20; 0.48	0.08	32
LDL (mg/dL)	20	-0.30 [-0.40; -0.20]*	-0.41; -0.19	0.77	0
Triglycerides (mg/dL)	20	0.02 [-0.12; 0.17]	-0.46; 0.51	<0.01	48
BMI (kg/m ²)	14	-0.04 [-0.15; 0.08]	-0.16; 0.09	0.84	0

Subgroup Results

The subgroup analysis included the duration of the intervention, type of intervention, comparison/control group, and study quality. Type of intervention (p =0.02). and the comparison/control group (p =0.01) showed

significant differences in the effect of the low GI intervention on HbA1c levels. Comparison/control (p = 0.002) and quality of research (p = 0.02) caused significant differences in the effect of low GI intervention on HDL (Table 2).

Table 2. Subgroup outcome HbA1c, HDL, LDL, triglycerides and BMI

Subgroup	HbA1c	HDL	LDL	Triglycerides	BMI
Duration:	0.11	0.69	0.64	0.49	0.31
<8 weeks	-0.27 [-0.39; -0.14]	0.09** [-0.06; 0.25]	-0.26** [-0.39; -0.13]	0.09 [-0.14; 0.32]	0.01** [-0.13; 0.15]
8-12 weeks	-0.48** [-0.65; -0.32]	0.20 [-0.06; 0.46]	-0.35* [-0.53; -0.17]	-0.09* [-0.27; 0.10]	-0.18** [-0.40; 0.04]
>12 weeks	-0.52 [-1.17; 0.14]	0.21** [-0.11; 0.54]	-0.38** [-0.71; -0.05]	0.03** [-0.29; 0.36]	0.05 [-0.33; 0.42]
Type of Intervention:	0.02*	0.06	0.56	0.06	0.10
Supplementation	-0.58** [-0.74; -0.41]	0.31 [0.08; 0.53]	-0.34** [-0.52; -0.17]	-0.14** [-0.31; 0.04]	-0.29** [-0.55; -0.03]
Supplementation and Nutrition Counseling	-0.35 [-0.96; 0.26]	-	-	-	-0.05 [-0.66; 0.56]
Food	-0.38 [-0.51; -0.25]	0.05** [-0.09; 0.19]	-0.28** [-0.40; -0.16]	0.11 [-0.08; 0.31]	0.03** [-0.10; 0.15]

Control:	0.01*	0.002*	0.50	0.59	0.49
Usual Diet and Usual Physical Activity	-1.00	-	-	-	-0.41*
Nutrition Advice	0.35	-	-	-	-0.05
	[-0.96; 0.26]				[-0.66; 0.56]
Usual Diet	-0.37	0.00**	-0.35**	-0.01	0.14**
	[-0.64; -0.10]	[-0.17; 0.17]	[-0.52; -0.18]	[-0.29; 0.28]	[-0.06; 0.34]
Diabetes Diet, Exercise Therapy, and Oral Hypoglycemic Drugs	-0.70	-	-	-	-
NCEP Step II Diet	-0.10	-0.12	-0.27	0.19	-0.09
	[-0.58; 0.38]	[-0.61; 0.36]	[-0.75; 0.22]	[-0.30; 0.67]	[-0.58; 0.39]
White Rice	-0.18	-0.28	-0.21	0.03	-0.03
	[-0.92; 0.57]	[-1.03; 0.46]	[-0.96; 0.53]	[-0.71; 0.77]	[-0.77; 0.71]
Healthy Breakfast	-0.61	-0.26	0.14	0.39	-0.27
	[-1.19; -0.03]	[-0.83; 0.31]	[-0.43; 0.70]	[-0.18; 0.96]	[-0.83; 0.30]
Low Fat and High Fiber	-0.24**	0.30**	-0.23**	0.37	-0.07**
	[-0.46; -0.02]	[0.08; 0.52]	[-0.45; -0.01]	[-0.36; 1.10]	[-0.29; 0.15]
Rice Flour and Wheat Flour	-0.24	-0.04**	-0.14	-0.03**	-0.00
	[-0.65; 0.16]	[-0.32; 0.23]	[-0.42; 0.13]	[-0.30; 0.25]	[-0.31; 0.30]
Red Meat	0.29**	-0.05**	-0.40**	-0.23**	-
	[-0.13; 0.72]	[-0.47; 0.37]	[-0.83; 0.02]	[-0.65; 0.19]	
Placebo	-0.54**	0.52**	-0.45**	-0.12**	-0.21**
	[-0.77; -0.32]	[0.29; 0.75]	[-0.68; -0.23]	[-0.34; 0.10]	[-0.60; 0.18]
Quality of Study: Good	0.30	0.02*	0.50	0.05	0.33
	-0.52**	0.36**	-0.40**	-0.19**	-0.26**
	[-0.70; -0.35]	[0.15; 0.58]	[-0.58; -0.21]	[-0.38; -0.01]	[-0.59; 0.06]
Moderate	-0.31	0.06**	-0.26**	0.16	0.00**
	[-0.52; -0.10]	[-0.11; 0.23]	[-0.40; -0.13]	[-0.07; 0.39]	[-0.13; 0.14]
Poor	-0.35	-0.06**	-0.27**	0.05**	-0.03**
	[-0.89; 0.19]	[-0.30; 0.18]	[-0.51; -0.02]	[-0.19; 0.29]	[-0.29; 0.23]

Note: standard mean difference, 95%CI; *significant p-value < 0.05; **heterogeneity $I^2 < 30\%$; -no study

Meta Regression Results

Meta-regression was performed on each outcome by considering moderators such as mean age, percent of female, duration of intervention, type of intervention, and study quality. The moderators that significantly affected low GI on HbA1c were the percentage of women and the type of intervention. The greater the number of female participants, the weaker

the effect of low GI on HbA1c 1.22 with an estimated range of 95% CI [0.18, 2.26] compared to men.

While the intervention was in the form of supplementation compared to the form of food, the effect of giving low GI on HbA1c was stronger 0.77 with an estimated range of 95% CI [-1.36, -0.18] (Table 3).

Table 3. Meta-Regression of HbA1c, HDL, LDL, triglycerides, and BMI

Sub Group	HbA1c	HDL	LDL	Triglycerides	BMI
Percentage of Female	1.22* [0.18; 2.26]	0.98 [-0.08; 2.05]	-0.98 [-1.98; 0.02]	0.09 [-1.17; 1.35]	-0.88 [-4.05; 2.29]
Duration of Intervention:					
<8 weeks	REF	REF	REF	REF	REF
8-12 weeks	0.16 [-0.16; 0.49]	0.00 [-0.35; 0.35]	-0.18 [-0.51; 0.14]	-0.02 [-0.44; 0.39]	-0.01 [-0.39; 0.37]
>12 weeks	-0.24	0.11	-0.05	-0.13	0.15

Type of Intervention:	[-0.56; 0.07]	[-0.29; 0.51]	[-0.42; 0.31]	[-0.64; 0.37]	[-0.53; 0.83]
Supplementation	-0.77*	-0.19	0.46	0.26	-0.40
Supplementation and Nutrition Counseling	[-1.36; -0.18]	[-0.90; 0.51]	[-0.20; 1.12]	[-0.57; 1.09]	[-1.00; 0.20]
Food	-0.27	-	-	-	-0.08
Quality of Study:	[-1.00; 0.46]	REF	REF	REF	REF
Good	REF	REF	REF	REF	REF
Moderate	-0.05	-0.27	0.23	0.61	-0.39
Poor	[-0.66; 0.55]	[-1.00; 0.46]	[-0.46; 0.92]	[-0.25; 1.48]	[-1.68; 0.90]
	-0.19	-0.47	0.35	0.51	-0.35
	[-0.86; 0.47]	[-1.25; 0.30]	[-0.37; 1.07]	[-0.43; 1.46]	[-1.36; 0.66]

Note: Estimated SMD; 95%CI; *significant p -value <0.05 ; - could not be analyzed because the number of studies differs from others; REF=reference.

Evaluation of Publication Bias

The outcomes of HbA1c ($p = 0.1212$), HDL ($p = 0.6424$), LDL ($p = 0.7181$), and triglyceride ($p = 0.0887$) levels showed no publication bias in this study. For BMI, there was a publication bias ($p = 0.0189$) after trimming and filling ($p = 0.8716$).

$p = 0.0887$) levels showed no publication bias in this study. For BMI, there was a publication bias ($p = 0.0189$) after trimming and filling ($p = 0.8716$).

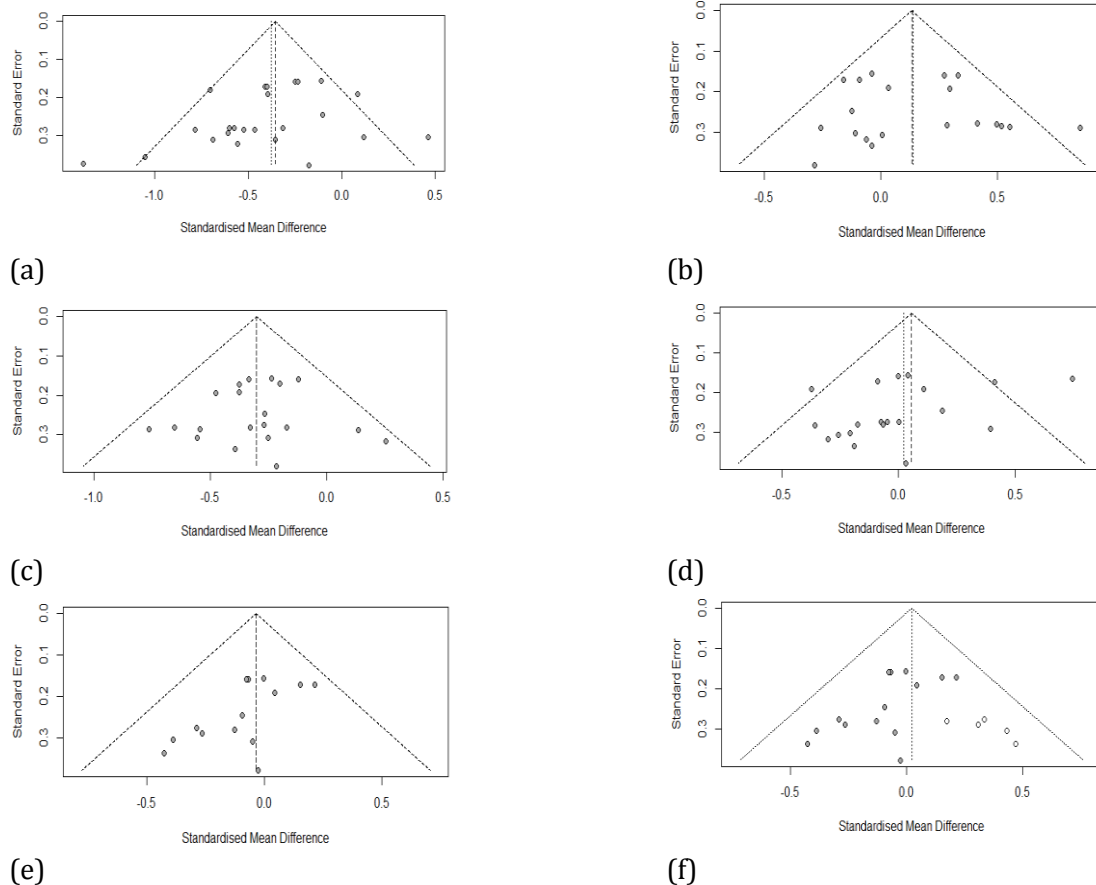


Figure 2. Funnel Plot (a) HbA1c; (b) HDL; (c) LDL; (d) Triglyceride; (e) BMI; and (f) BMI after Trim and Fill.

Quality of Study

This systematic review and meta-analysis included 16 studies (100%) using a Randomized Controlled Trial (RCT) study design. Research

quality assessment using Risk of Bias 2 (ROB-2). Five studies had a low risk of bias (31%), eight had a moderate risk of bias (50%), and three had a high risk of bias (19%) (Figure 3).

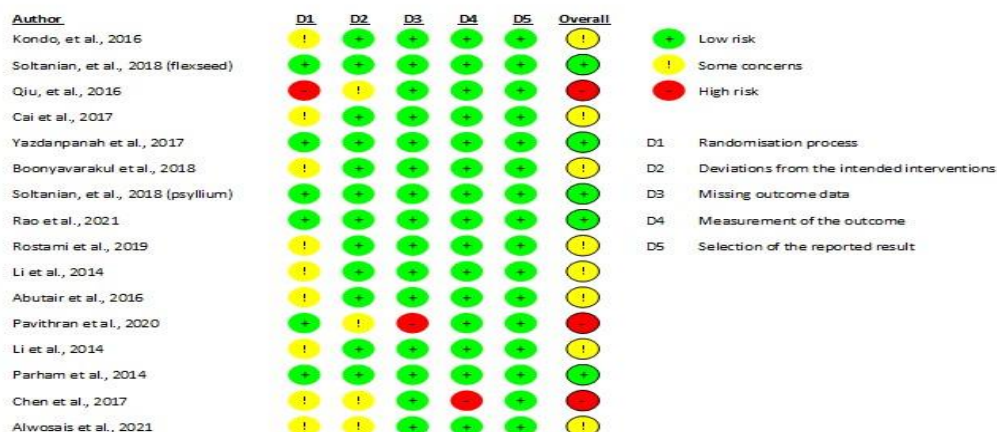


Figure 3. Quality of Study with ROB-2

Certainty of Evidence

This study reported low-to moderate-certainty evidence using GRADE. The outcomes of HbA1c, HDL, triglycerides, and BMI had a low level of evidence. The LDL outcome had a moderate level of evidence.

Overall, the level of certainty of the evidence for the various study outcomes varied. For HbA1c, HDL, and triglyceride outcomes, the evidence was downgraded by three levels due to the moderate-high risk of bias in most articles, inconsistency due to heterogeneity, and imprecision due to confidence limits that exceeded two-way effect sizes. However, the certainty of evidence was subsequently raised by one level as all studies were RCTs, and therefore, the potential for confounding was minimal. Therefore, the final certainty level for this outcome was low.

For the LDL outcome, the evidence was downgraded by two levels due to moderate-high risk of bias and imprecision, and then upgraded by one level as all studies were RCTs. The final result showed a moderate level of evidence certainty.

Meanwhile, for the IMT outcome, the evidence was downgraded by three levels due to the high proportion of articles with moderate-to-high risk of bias, imprecision, and indications of publication bias. Similar to other outcomes, the certainty of evidence was raised by one level because all the studies were RCTs. Therefore, the final certainty level for this outcome was low.

Effect of Low Glycemic Index (IG) Diet on HbA1c

The results of this study are in line with those of Zafar et al. (2019), who found a decrease in

HbA1c of MD -0.19% with an estimated range of 95%CI [-0.28, -0.11], but did not have heterogeneity ($I^2 = 1\%$). This is because the sample size used in this study was quite large. Low-GI diets have the potential to improve glycemic control in individuals with diabetes (Wang et al., 2015). According to the United Kingdom Prospective Diabetes Study, every 1% decrease in HbA1C reduces the risk of complications by 35%, the incidence of death by 21%, myocardial infarction by 14%, microvascular complications by 37%, and peripheral vascular disease by 43% (Chugh et al., 2011 in Purwandari et al., 2022). In addition, several factors affect HbA1c, including abnormal hemoglobin, red blood cell synthesis (defective erythropoiesis), abnormal glycation, red blood cell damage, blood disorders, blood transfusions, and pregnancy (Rawal Gautam et al., 2016).

Low-GI supplementation can be an effective strategy to support dietary adherence with good practices that can improve glycemic control, especially HbA1c (Al-Salmi et al., 2022). The study did not describe the usual diet of individuals with DM or the usual diet of healthy individuals. Physical activity was not included in the form of recommended physical activity or activity for healthy individuals. Therefore, further research is needed to compare diet with details, duration, and type of physical activity performed.

The percentage of females significantly affected the low GI of HbA1c. Females can increase the likelihood of poor glycemic control by 2.7 times (AOR = 2.7, 95% CI: 1.23, 6.15) compared to men (Shibabaw et al., 2023). This could be due to insulin resistance that occurs after menopause. Diabetic females are more

likely to lose glucose homeostasis after menopause (Duarte et al., 2019). Decreased estrogen levels in postmenopausal women can accelerate the development of insulin resistance and T2DM (Louet et al., 2004, Yan et al., 2019). This emphasizes that future research should consider sex distribution in study design and analysis, as it may impact the estimates of the effectiveness of dietary interventions. From a policy perspective, diabetes management programs should adopt gender-responsive strategies, tailoring interventions to the specific needs of women, especially postmenopausal women, who are more vulnerable to insulin resistance and poor glycemic control.

Another moderating factor that significantly influenced low HbA1c values was the type of intervention in the form of supplementation. People with DM2 often have poor dietary compliance; therefore, efforts are needed to set practical goals (Al-Salmi et al., 2022). Low-GI supplements can be an effective strategy for supporting dietary compliance with good practices, thereby improving glycemic control, especially HbA1c. Low-GI food supplementation is assumed to be more practical; it contains sufficient low-GI content in small volumes, lacks unwanted additives such as fat, cholesterol, and purines, and supplementation in powder form has relatively rapid absorption (Hassan et al., 2020).

There was no difference in the duration of the low-GI intervention on HbA1c; therefore, an intervention duration of 8-12 weeks can be used as an option (Reynolds & Mitri, 2024). Although some results were statistically significant, the small effect size (low SMD) may not be clinically relevant. Therefore, it is important to distinguish between statistical and clinical significance when interpreting the findings.

Effect of Low Glycemic Index (IG) Diet on HDL

The results of this study contradict those of previous research showing that a low-GI diet has no effect on HDL cholesterol (Goff et al., 2013 in Ojo et al., 2019). Epidemiological studies have shown that HDL is inversely related to the risk of cardiovascular events (Emerging Risk Factors Collaboration, 2009). In this study, a low GI diet increased HDL levels by 0.14 mg/dL, which is expected to help reduce the risk of cardiovascular disease in individuals with T2DM. Low GI interventions had a greater effect on increasing HDL levels in populations with

good research quality, with an SMD of 0.36 mg/dL. In this study, good research quality requires attention to the randomization process, blinding, explanation of missing data, and process of measuring outcomes (Higgins JPT et al., 2023).

Effect of Low Glycemic Index (GI) Diet on LDL

The results of this study are in line with previous research showing that a low-GI diet can help reduce LDL cholesterol (Fleming & Godwin, 2013). Regarding weight maintenance, the low-GI diet led to greater reductions in serum total cholesterol and fasting LDL levels. The higher fiber content of the low-GI diet and reduced cholesterol consumption support reduced fat absorption and lower hepatic cholesterol synthesis, which contributed to the reduced circulating lipids. Low-GI diets also support insulin sensitivity (Zhang et al., 2010).

Effect of Low Glycemic Index (GI) Diet on Triglycerides

The increase in triglyceride levels after the administration of the low-GI diet in this study may be due to the nutritional status of the participants with T2DM.

The relationship between dietary GI and serum triglyceride levels was more pronounced in overweight individuals. Dietary GI and fasting triglyceride levels have a stronger relationship in overweight women (Ford et al., 2001, Pelkman, 2001). There are factors that influence the response to changes in fat, carbohydrate, and cholesterol in food, such as the presence of specific genetic polymorphisms (Schaefer et al., 1997; Ye & Kwiterovich, 2000; Erkkilä et al., 2001), the amount and distribution of body fat, and the initial concentrations of lipids and lipoproteins (Jensin et al., 1998 and Denke et al., 1995 in Pelkman, 2001). The results of this study had a limited number of studies that showed significant heterogeneity. In addition, this study did not consider nutritional status, amount, or distribution of body fat.

Effect of Low Glycemic Index (IG) Diet on BMI

This study is in line with previous research, namely 22 studies showing a decrease in BMI associated with a low GI diet (SMD -0.16 kg/m² with an estimated range of 95%CI [-0.28, -0.04])(Zafar et al., 2019). Low-GI diets tend to be high in fiber content. Fibers can slow down the rate of food in the digestive tract and inhibit

enzyme activity, so that the digestive process, especially starch digestion, becomes slow, and the blood glucose response will be lower (Jenkins et al., 2002 in Arif et al., 2014). Increased fiber consumption can reduce BMI by MD -0.36 kg/m² with 95%CI estimate range [-0.55; -0.16 from 14 studies] (Reynolds et al., 2020).

Low-GI diets may be useful for glycemic control and may reduce body weight in individuals with prediabetes or diabetes in Asia (Zafar, Mohammad Ishraq; Kerry E Mills; Zheng, Juan; Mills, Kerry E; Zheng & Regmi, Anita; Hu, Sheng Qing; Gou, Luoning; Chen, 2019). Meanwhile, a study in Europe showed that low GI/GL diets provide modest but clinically meaningful benefits, including reductions in HbA1c and improvements in cardiometabolic risk factors, such as blood lipids, weight, blood pressure, and inflammation in type 1 and type 2 diabetes. These effects are observed beyond standard drug or insulin therapy, highlighting their potential as adjunctive dietary strategies (Chiavaroli et al., 2021).

This study has several limitations that should be considered when interpreting the results. This study has limitations, including low to moderate certainty evidence, heterogeneity, and language limitations, as it only uses English, has a limited geographic spread, and only uses 3 databases for data search.

Conclusion

A low glycemic index diet can reduce HbA1c, increase HDL, decrease LDL, increase triglycerides, and decrease body mass index in people with type 2 diabetes mellitus in the Asian continent, although the triglyceride and BMI outcomes failed to be meaningfully significant. There was a significant difference in the low glycemic index diet on HbA1c in the type of intervention and comparison/control groups. There was a significant difference in the effect of the low glycemic index diet on HDL in the comparison/control group and study quality. The moderators that affected the effect of the low-GI diet on HbA1c were the percentage of females and the type of intervention. Although some results were statistically significant, their small effect size (low SMD) and the presence of heterogeneity, along with the low-to-moderate certainty of evidence (GRADE), suggest limited clinical relevance and highlight the need to

distinguish between statistical and clinical significance when interpreting the findings.

A low glycemic index (GI) diet can be an effective alternative for managing type 2 diabetes mellitus (T2DM), supporting better glycemic control, and reducing the risk of cardiovascular complications. Future research should include articles in local languages, expand database searches, and consider additional populations, such as pregnant, breastfeeding, and menopausal women. Primary studies should improve reporting on the duration of T2DM, duration and type of T2DM treatment, missing data, explanation of outcome measurements, explanation of specific interventions and control, randomization, blinding process appropriately, increase the sample size, and consider potential moderators (type of low GI intervention in the form of supplementation and percentage of females), use a comparison/control in the form of a high glycemic index, long duration of intervention for 8-12 weeks; and nutritional status, body composition, stress factors, diet, and menopausal events.

In clinical practice, low-GI diets can support standard T2DM management and cardiometabolic risk prevention. However, due to the low certainty of evidence and possible influence of sex or supplementation type, standard therapy should remain the primary approach. These findings provide preliminary support for policymakers to incorporate low-GI diets into health promotion strategies for T2DM management.

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