ENDOCRINOLOGY RESEARCH AND PRACTICE

SOCIETY OF ENDOCRINOLOGY AND METABOLISM OF TURKEY

REVIEW
Endocrinol Res Pract. 2025;29(3):250-260

Interventions to Prevent Type 2 Diabetes Mellitus in Women with History of Gestational Diabetes Mellitus, in a Low Resource Setting-A Systematic Review

ABSTRACT

Type 2 diabetes mellitus (T2DM) is more likely to strike women who have previously had gestational diabetes mellitus (GDM) in the near future. There are no proper review articles comparing all the types of intervention (breastfeeding, diet, physical exercise, etc.) which are cost-effective and feasible. The aim of this study was to review published interventions to prevent T2DM in women with history of GDM in a low-resource setting. A detailed literature search was conducted and among the 1833 articles identified, 9 were selected for review following PRISMA guidelines. These studies were evaluated with the Cochrane risk of bias tool, and any discrepancies were resolved. A thematic narrative approach was used for the generation of results and analysis. This review identified the cost-effective interventions like breastfeeding, drugs like Metformin, physical exercise, health educational intervention by using Health Belief Model, lifestyle changes, Mediterranean diet, nutritional pattern and were effective in prevention/delay in the incidence of T2DM. Barriers need to be overcome, and support needs to be provided to implement necessary screening and low-cost feasible interventions to prevent T2DM in this high-risk population at the correct window of opportunity.

Keywords: Cost-effective, gestational diabetes mellitus, intervention, prevention, type 2 diabetes mellitus

Introduction

Gestational diabetes mellitus (GDM) is defined as "any degree of glucose intolerance with onset or first recognition during pregnancy" by the American Diabetes Association (ADA).[1] Gestational diabetes mellitus is one of the most frequent pregnancy-related problems, with an incidence of 5.8%-12.9% globally.[2] In low- or middle-income nations with limited access to prenatal care, the majority of GDM cases (84%) are reported.[3] The GDM prevalence is on the rise in India, much like that of diabetes mellitus.[4]

About 50% of women with a history of GDM are susceptible to type 2 diabetes 5-10 years after giving birth.[5] A recent study conducted in Chennai (India), showed that 20% of GDM women had glucose intolerance within 1 year after delivery, and 12% were glucose intolerant within 6-12 weeks after delivery.[6] In comparison to neighboring nations like Bangladesh (9.8%) and Sri Lanka (9.9%), India demonstrated a high estimated incidence of GDM (27.5%), according to a study by Gauriguata et al (2015).[7] A study by Christina et al[8] depicts that family history of diabetes and poor glycemic control during pregnancy had a strong association with the development of type 2 diabetes mellitus (T2DM) after delivery. In comparison to a normoglycemic pregnancy, a meta-analysis estimated that the relative risk of acquiring T2DM following GDM was 4.69 during the first 5 years after birth and 9.34 beyond 5 years.[9] Similarly, a systematic review discovered that among women with prior GDM, the cumulative incidence of T2DM increased quickly in the first 5 years following birth and plateaued after 10 years.[10]

Poorly managed GDM leads to many complications, including early onset of T2DM. Being diabetic in middle age affects personal health, sources of income and the economy. Hence, timely, cost-effective interventions must be implemented, focusing this high-risk population.

Countries with low-income/middle-income need more cost-effective interventions that target pregnant women with a history of GDM to prevent diabetes mellitus in the future.

Arun Murugan
Ramachandran Ramasubramanian
Kasinathan Sathish Kumar
Gnanavel Pavithra
Premnath Arulmozhi

Department of Community Medicine, Government Omandurar Medical College, Tamil Nadu, India

Corresponding author:
Kasinathan Sathishkumar
✉ kumarsathish16@gmail.com

Received: August 28, 2024
Revision Requested: September 16, 2024
Last Revision Received: January 28, 2025
Accepted: February 5, 2025
Publication Date: April 15, 2025

Cite this article as: S, Arunmurugan, Ramasubramanian R, Sathish Kumar K, Pavithra G, Arulmozhi P. Interventions to prevent type 2 diabetes mellitus in women with history of gestational diabetes mellitus in A low resource setting-A systematic review. *Endocrinol Res Pract.* 2025;29(3):250-260.

DOI: 10.5152/erp.2025.24543

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Some of the available low-cost interventions include health education, lifestyle modification, dietary changes, exercise, postpartum weight control management and health-promoting interventions, exclusive breastfeeding, and targeted pharmacological interventions.

Material and Methods

This study aims to assess documented strategies for GDM prevention or delay in low-income and resource-constrained women with a history of the disease. The review was proactively registered on PROSPERO (Prospective Register of Systematic Reviews–registration number CRD42023442920). A 3-stage approach was used for the study. Firstly, a systematic literature review was done following PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines. Secondly, the studies selected were appraised for quality using the Revised Cochrane risk of Bias Tool (RoB-2 version, 22 August 2019). Finally, the findings of each study were thematically analyzed and compared.

Figure 1 indicates the PRISMA flowchart outlining search strategy and results. A detailed literature search was done in PubMed, Cochrane Library, CINAHL (EBSCO), and EMBASE databases. Key search items (both words in MESH (Medical Subject Heading) database and text word items to retrieve all relevant studies) were used, including gestational diabetes, GDM, intervention, T2DM, diabetes prevention, pre-diabetes, strategy, diet, program, and lifestyle. A total of 1833 studies were identified through database searching and data, including the abstracts, pooled to an Excel sheet using ENDNOTE software trial version. A total of 138 studies were identified as duplicates and excluded. Publication dates were limited to 2010 onward, because the largest contemporary search was limited to this period and 1594 studies were included for primary screening.

Inclusion criteria were studies published in the English language, studies done on humans, interventional studies (RCT or Cohort), women previously diagnosed with GDM (study population), behavioral or pharmacological interventions (which were feasible to implement in low-income or low-resource settings) to prevent or delay the risk of T2DM (intervention and outcome), peer-reviewed and professional publications (source), studies published from 2010 onward (publication time period).

Studies done in animals, papers presented in conferences, study protocol without results and discussions were excluded.

The preliminary search that yielded 1594 articles was screened based on title and abstract by 2 authors (Arun Murugan (AM) and Kasinathan Sathishkumar (KS) independently) and resolved discrepancies by consensus. A total of 1565 publications were removed because they did not match the inclusion criteria, and 29 full-text articles were reassessed by both authors for eligibility (quality and relevance), which was followed by agreement and co-assessment. Nine studies were then selected for analysis. Though the studies included interventions that were done in developed countries, the pharmacological and behavioral changes that were mentioned in the studies were feasible to be implemented in a low-income and low-resource setting. A narrative approach was used to synthesize the evidence for the research question.

MAIN POINTS

- Poorly managed GDM leads to complications, including early onset of T2DM.
- Interventions related to lifestyle, social and professional assistance may help to enhance mother and infant health.
- Early intervention, ideally with in-person recruiting, can boost screening participation and assist women in adopting healthy lifestyles.

Results

Table 1 shows: The selected 9 studies were evaluated for methodological rigor using the Revised Cochrane Risk of Bias Tool (RoB2 version 2019). Two of the studies were cohort study designs, so some of the assessment domains were not available/applicable (NA). The tool included assessment of quality in 5 domains: [1. DOMAIN 1 (selection bias)—Random sequence generation/Allocation concealment, 2. DOMAIN 2 (performance bias)—Blinding of participants, 3. DOMAIN 3 (attrition bias)—Incomplete outcome data, 4. DOMAIN 4 (detection of bias)—method of measuring appropriate outcome, blinding of outcome assessment, 5. DOMAIN 5 (reporting bias)—Selective reporting]. The first and second author independently assessed the quality of the studies, and any disagreements were resolved by consensus. The overall risk of bias was low for all the selected studies, so they were included in the systematic review. A meta-analysis could not be justified, as the outcome measurements of the studies were not uniform. Therefore, a thematic narrative method was used for the discussion and results.

The characteristics of the 9 studies included are described in Table 2. The focused areas of intervention in all the studies are feasible and can be applied in a low resource setting for the prevention of T2DM in women with previous history of GDM. Of the 9 studies, 2 studies focused on breastfeeding,[11,12] 2 studies focused on pharmacological intervention (drugs),[13,14] 5 studies focused on lifestyle intervention[15-18,19] (diet, exercise, and health education).

The selected studies were found to be published in the time period 2012-2023 and in countries like the United States of America (n = 3),[11,13,17] Germany (n = 2),[12,14] Egypt (n = 1),[15] China (n = 1),[16] India (n = 1),[1] and Malaysia (n = 1).[18] Every study featured a well-defined population selection (women with a history of GDM), a targeted intervention location and kind, a follow-up time of 1-19 years, and a primary outcome measure that was centered on avoiding or postponing the onset of T2DM.

The Table 3 describes the results and outcomes measured from all 9 studies. Six of the studies were fully completed fully and yielded positive results in preventing or delaying the onset of T2DM. One study (Hummel et al, 2017[14]) was terminated due to a low diabetes rate in the outcome, and their results showed no significant superiority of the drug Vildagliptin over placebo.[14]

Discussion

This review identified the cost-effective interventions like breastfeeding, drugs like Metformin, physical exercise, health educational intervention by using Health Belief Model, lifestyle changes, Mediterranean diet, nutritional pattern and were effective in prevention/delay in the incidence of T2DM.

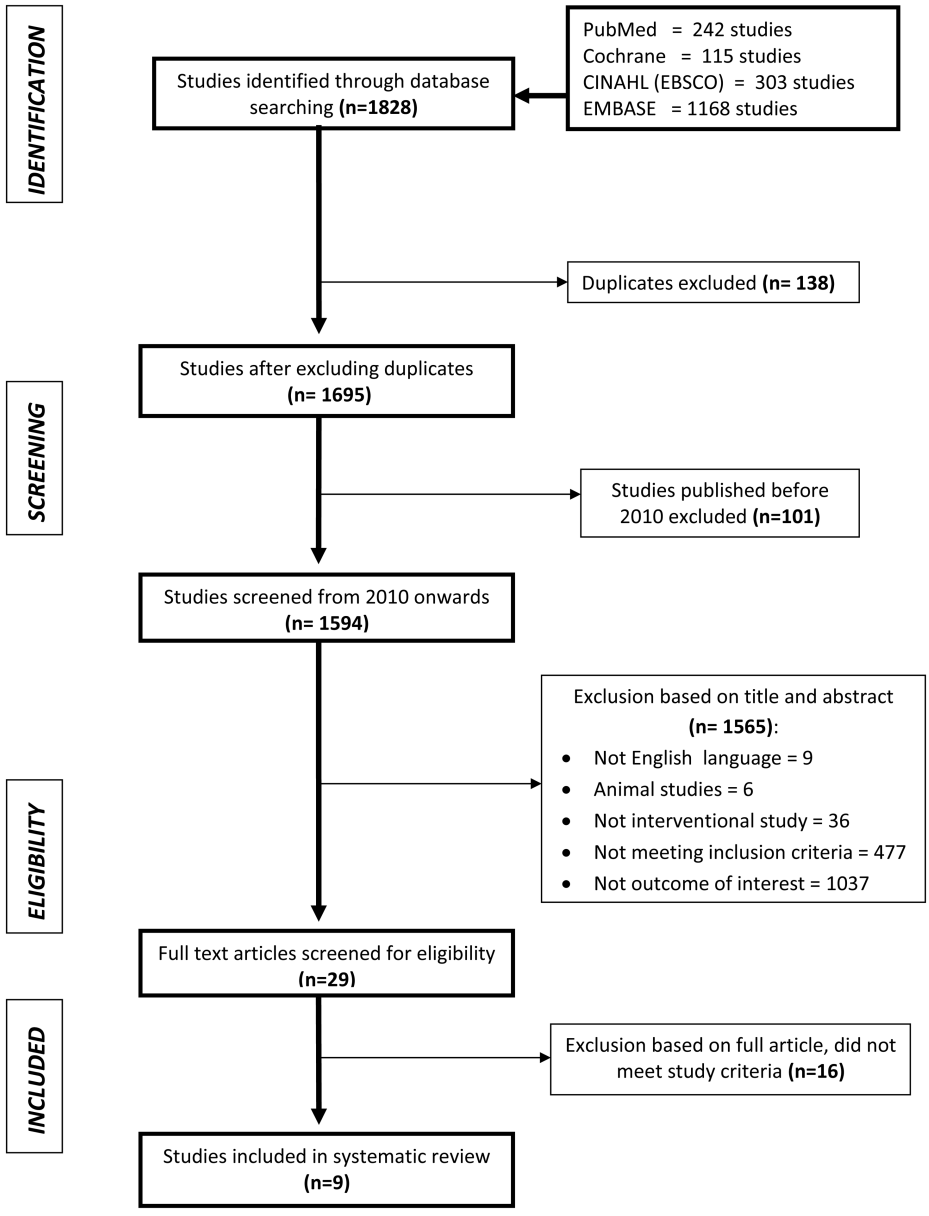

Figure 1. PRISMA flowchart outlining search strategy and results.

According to the analysis of the studies, exclusive breastfeeding and prolonged breastfeeding greatly lowered the chance of developing diabetes or prediabetes. ($P < .05$).[11,12] Similarly, Kjos et al's[20] retrospective cohort research revealed that Latinas in the breastfeeding (any intensity) group had fasting blood glucose levels that were 5 mg/dL lower than those in the no lactation group. McManus et al[21] in their study had reported improved glucose tolerance and insulin response in lactating women (3 months postpartum) with a history of recent GDM. However, the study's limited sample size prevented statistical significance from being established. The incidence of postpartum diabetes was negatively correlated with the length of breastfeeding (>3 months) ($P = .002$)[12] [had a longer time without diabetes—about 18.2 years]. Although there may be confounding effects from postpartum lifestyle changes, breastfeeding for at least three months improves glucose and lipid metabolism and offers some direct protection against diabetes.[20] A team of researchers in South Korea discovered that through the generation of serotonin, lactation boosts the mass and activity of pancreatic beta cells. In addition, intracellular serotonin acted as an antioxidant to mitigate oxidative stress and improve β cell survival.[22]

During a 10-year follow-up period, intensive lifestyle adjustment (weight reduction and moderate-intensity physical exercise) along with pharmacological management with Metformin lowered the incidence of eventual diabetes in this high-risk group.[13] A similar study in a Diabetes Prevention Program/Diabetes Prevention Program Outcome Study cohort at 10 years showed an overall 18% risk reduction with Metformin, suggesting that people with a history of GDM represent a high-risk group that can benefit from Metformin therapy.[23] While Vildagliptin did not show any superiority over placebo in a study done by Hummel et al,[14] following the expiration of its patent and a 70% cost reduction in 2019, it is being extensively utilized in low- and middle-income nations like India.[24]

Table 1. Revised Cochrane Risk-of-Bias Tool (RoB 2—Version of August 22, 2019)

Studies	DOMAIN 1 (Selection Bias)		DOMAIN 2 (Performance Bias)	DOMAIN 3 (Attrition Bias)	DOMAIN 4 (Detection Bias)		DOMAIN 5 (Reporting Bias)	Overall Risk of Bias
	Random Sequence Generation	*Allocation Concealment*	*Blinding of Participants and Personnel*	*Incomplete Outcome Data*	*Method of Measuring Outcome Appropriate*	*Blinding of Outcome Assessment*	*Selective Reporting*	*Risk of Bias Judgement*
1) Gunderson et. al—[2012] (cohort)	NA	NA	NA	+	+	NA	+	+
2) Zeigler et al—[2012] (cohort)	NA	NA	NA	+	+	NA	+	+
3) Aroda et. al—[2014] (RCT)	+	+	+	+	+	NA	+	+
4) Hummel et al—[2017] (RCT)	+	+	+	?	+	?	+	+
5) Mirella Youssef Tawfik—2016 (RCT)[15]	+	+	+	+	?	+	+	+
6) Liang et al—[2019] (RCT)	+	+	?	+	+	?	+	+
7) Perez-Ferre et al—[2014] (RCT)	+	+	?	+	+	?	+	+
8) Lee et al—[2022] (RCT)	+	+	NA	-	+	NA	NA	+
9) Tandon et al—[2022] (RCT)	+	-	-	-	+	NA	-	-

+ : Low risk of bias ? : Unclear Risk of bias: High risk of bias NA : Not assessed.

According to a study by Tawfik et al,[15] there is a prevention risk for T2DM with health educational intervention based on the health belief model (HBM) [health educational intervention on knowledge, beliefs, and self-reported practices, exclusive breastfeeding, postpartum body weight].

A healthy lifestyle intervention improved insulin resistance in women with previous GDM (with a CDKAL1 mutation), according to a study by Liang et al.[16] Though genetic screening is not feasible in a low-resource setting, lifestyle intervention (improved physical activity and diet patterns) is definitely possible in postpartum mothers with a history of GDM. Additionally, a recent retrospective study found that among women with a history of GDM,[25] there was an inverse relationship between the development of T2DM and a healthy dietary pattern. Particular attention is paid to preventing diabetes through dietary habits.[26,27]

In women with a history of GDM, a Mediterranean diet rich in fruits, vegetables, legumes, nuts, and olive oil with less red meat and physical activity has been shown to be protective against glucose problems.[17] A collection of studies showed that dietary factors regulate insulin sensitivity[28-30]

Since there was no difference in the incidence of type 2 diabetes between the intervention and control groups, Lee et al[18] concluded that the system-based intervention based on behavioral change communication was not statistically superior to the control intervention. According to a study by Tandon et al,[19] a pragmatic lifestyle intervention was unable to prevent glycemic worsening among women with recent GDM in South Asian metropolitan settings.

A 30% reduction in fat consumption relative to caloric intake might significantly change insulin sensitivity.[30] Furthermore, increased exercise or physical activity can enhance insulin control and glucose metabolism.[31] Therefore, combining physical exercise with better eating practices would benefit insulin sensitivity and glucose metabolism.

The review proposed interventions that are cost effective and feasible to be applied in low/middle-income countries and low-resource settings like India. The interventions that were potentially considered included exclusive and long-duration breastfeeding, health education for behavioral change, pharmacological intervention (Metformin), and lifestyle modification with improved physical activity and dietary patterns (healthy diet habits, Mediterranean diet, etc.) with regard to T2DM prevention in women with previous GDM. After an in-depth literature review, it is found that almost all the studies published in this area were conducted in developed nations. Further high-quality interventional research should be encouraged in developing countries for the systematic development of policy guidelines to prevent diabetes in this high-risk population at a correct window of opportunity.

Articles from genuine, high-quality databases like PUBMED, COCHRANE, EMBASE, etc have been screened. Trials measuring the effect on biomarkers of insulin resistance/sensitivity, in addition to blood glucose levels, have been included. The selected 10 studies were conducted in developed countries whose ethnicity and genes may vary from those in developing countries. The outcomes or results may vary, and external validity may be affected with a potential risk of bias in both directions.

Table 2. Characteristics of the Studies Included in Systematic Review

First Author and Year of Publication	Country, Study Design	Time Frame, Number of Participants	Inclusion Criterion in Addition to History of GDM	Focus Area of Intervention	Primary Intervention	Assessments	Primary Outcome
1) Gunderson et al[11] 2012	Northern California, Cohort design	September 2008-March 2011, n = 522	Study of women, infant feeding, and development of type 2 diabetes (SWIFT), delivered a singleton, live birth ≥35 weeks gestation, were free of diabetes at 6-9 weeks' postpartum	duration and intensity of **breastfeeding** and formula feeding	exclusive or mostly breastfeeding (giving ≤6 oz formula per 24 hours) and exclusive or mostly formula feeding (giving ≥14 oz formula per 24 hours)	3-h 100-g OGTT (24-32 weeks gestation-GDM diagnosis) infant feeding practices telephonic interview (4-6 weeks postpartum) inquiry by research staff (6-9 weeks postpartum)	Fasting and 2-hour 75-g OGTT (6–9 weeks postpartum) Insulin sensitivity (ISI), Insulin (double-antibody radioimmunoassay and resistance indices (HOMA-IR)
2) Zeigler et al[12] 2012	Germany, Cohort design.	Recruited between 1989 and 1999: follow-up 19 years, n = 304	-	breastfeeding	lactation (yes/no), {the duration of lactation, and full lactation in postpartum till 9 months or 2 years (if the mother continues to feed till 2 years.)}	OGTT (GDM diagnosis) OGTT at 2 and 9 months; 2, 5, 8, 11, 15, and 19 years after pregnancy or until the diagnosis of diabetes. Questionnaire (lactation—duration, full lactation—child at 9 months or 2 years)	(ADA criteria) unequivocal hyperglycemia with acute metabolic decompensation / a 2-hour plasma glucose level >200 mg/dL after an oral GCT. A random blood glucose level >200 mg/dL if accompanied by unequivocal symptoms (clinical)
3) Aroda et al[13] 2014	27 clinical centres in the United States, RCT with an observational follow-up.	10 years [Enrollment began in July 1996 and ended in May 1999] [n = 350 history of GDM, n = 1416 no history of GDM]	at least 25 years of age and had a body mass index (BMI) of ≥24 kg/m^2 (≥22 kg/m^2 in Asian-Americans)	ILS (Intensive lifestyle), or metformin.	Participants divided into those with history and without history of GDM, were randomly assigned to one of 3 treatments: placebo + standard, nonintensive, lifestyle counseling—ILS, aiming for a 7% weight loss and ≥150 minutes of moderate intensity physical activity/week—850 mg metformin twice daily + standard, nonintensive, lifestyle counselling	The DPP and DPPOS design—OGTT (diagnosis of GDM) weight measurements, BMI self-reported activity levels using the Modifiable Activity Questionnaire adherence to metformin therapy, glucose, glycated hemoglobin (HbA1c), insulin levels	FBS levels measured every 6 months and 2-hour, 75-g OGTT conducted yearly. Diagnosis of diabetes was based on the ADA criteria. Insulin secretion estimated by the corrected insulin response: (100-30 minutes insulin) / [30 minutes glucose × (30 minutes glucose-70 mg/dL)]

(*Continued*)

Table 2. Characteristics of the Studies Included in Systematic Review (*Continued*)

First Author and Year of Publication	Country, Study Design	Time Frame, Number of Participants	Inclusion Criterion in Addition to History of GDM	Focus Area of Intervention	Primary Intervention	Assessments	Primary Outcome
4) Hummel et al[14] 2017	Munich–Neuherberg, Germany. (hospitals/ outpatient clinics) (Forschergruppe Diabetes e.V.,) RCT (investigator-initiated, phase II, single-center, randomized, double-blind, placebo-controlled trial)	2008-2015 113 patients (58 vildagliptin, 55 placebo) 2-year treatment period with 1 year follow-up	Females aged >18 years old, <9 months postpartum, and who had insulin-treated GDM during their most recent pregnancy	Pharmacological intervention: Vildagliptin (a dipeptidyl peptidase-4 inhibitor)	50 mg vildagliptin or placebo administered twice daily for 24 months followed by a 12-month observation period once a year standard lifestyle recommendations—annual, individualized consultation (based on the dietary reports provided by the women)	OGTT performed at baseline screening with blood samples drawn at −20, 0, 30, 60, 90, and 120 minutes (GDM Diagnosis) efficacy and safety assessments at 3, 6, 9, 12, 18, 24, 30, and 36 months. A standard meal challenge test performed at baseline, 24 and 36 months with blood samples drawn at −20, 0, 15, 30, 45, 60, 90, and 120 minutes. Compliance to lifestyle counseling—assessed at baseline, 12, 24, and 36 months. (Pedometer to record their steps for 7 consecutive days, food frequency questionnaire, daily energy and nutrient intake) Safety parameters-—AST, ALT, g-glutamyl transpeptidase, ALP, bilirubin, blood cell counts, creatinine, CK, Na, K, urea, uric acid, urine protein, pulse rate, and pregnancy tests at baseline, 3, 6, 9, 12, 18, 24, 30, and 36 months. Anthropometric measurements—height, weight, BMI, waist circumference, hip circumference.	OGTTs performed at 6, 12, 18, 24, 30, and 36 months with blood samples drawn at −20, 0, 30, 60, 90, and 120 minutes. Lab measurements insulin, pro-insulin, GIP, GLP 1, HbA1c
5) Mirella Youssef Tawfik[15] 2016	12 PHCs in 3 governorates in Egypt: (Ismailia, Port-Said and Suez) cluster randomized controlled trial (randomized at the level of PHCs)	September 2015-June 2016 235 (120 in intervention group, 115 received usual care)	≥24 weeks of gestation literate, 18-45 years of age, no history of chronic diseases or any other diseases which could interfere with the compliance according to the study protocol.	Health educational intervention—based on health belief model (HBM)	health belief model (HBM)-based educational intervention on knowledge, beliefs, self-reported practices, gestational and postpartum weight	GDM screening at ≥24 weeks gestation structured questionnaire (2 sections) First section—basic demographic and medical history data. Second section (7 domains)—for measuring knowledge, self-reported practices, and beliefs based on the HBM construct. Weight and height were measured using the balance beam scale.	1) Knowledge and beliefs – {At baseline 24 weeks gestation and 6 weeks postpartum} Knowledge (27 MCQ)—4 components: the risk factors, nature and screening, and preventive measures to develop T2DM. Beliefs-5 components: perceived susceptibility, severity, benefits, barriers and self-efficacy (likert scale). 2) Self-reported practices: {6 weeks postpartum} 2 closed-ended questions (Yes/No)—postpartum practice of exclusive breastfeeding and performing screening for T2DM. 3) Gestational weight gain: {baseline and before delivery}, pre-pregnancy weight computed and BMI calculated using it. 4) Postpartum weight reduction: {6 weeks postpartum}, absolute weight reduction computed.

First Author and Year of Publication	Country, Study Design	Time Frame, Number of Participants	Inclusion Criterion in Addition to History of GDM	Focus Area of Intervention	Primary Intervention	Assessments	Primary Outcome
6) Liang et al[16] 2019	Tianjin Womens and Children's Health Centre, Tianjin, China RCT	Baseline survey between August 2009 and July 2011 with 2 years intervention and follow-up. 1180 women (586 in lifestyle intervention group, 594 in control group)	Women aged 20 to 49 years at baseline survey, and diagnosed with GDM between July 2005 and June 2009. Exclusion criteria: Chronic diseases, diabetes at the screening visit, medications known to alter OGTTs, planning to be pregnant in the next 2 years were excluded	lifestyle intervention (improved physical activity and healthy dietary intakes)	In the first year: 6 face-to-face sessions with study dieticians and 2 telephone calls subsequent year: 2 individualized sessions and 4 telephone calls. The first year of the intervention (weight loss phase)—first 4 weeks dietary and physical activity intervention 4 weeks to 12th month-monitoring The lifestyle intervention included 5 goals: 1) reduction of 5%-10% of initial body weight for women with BMI ≥ 24 kg/m^2 by reducing at least 10% of total calories in their normal meal, and no weight loss for women with <24 kg/m^2 BMI 2) total fat intake <30% of energy consumed 3) carbohydrate intake 55%-65% 4) fiber intake 20-30 g/day 5) moderate /vigorous exercise for ≥30 minutes daily The second year: maintenance phase Control group: information on awareness of diabetes, dietary modification and physical activity given, while no specific individualized programs were offered.	GDM screening at 26-30 weeks gestation (WHO criteria)—[1 hour 50 g glucose screening test, 75 g 2 hour OGTT] At baseline survey: questionnaire {socio-demographic details, alcohol drinking, smoking habits, family h/o diabetes, dietary habits (self-administered food frequency questionnaire), physical activity (frequency and duration of 5 domains occupational, commuting, leisure time, household and sedentary activities)} The lifestyle changes —questionnaires on changes in major dietary and physical activity habits from the last visit. A 3-day 24-hours food record, and a self-administered annual questionnaire were completed at each annual visit.	At baseline and each visit-participants' body weight, height, waist and hip circumferences, BMI, body fat, fasting blood glucose, fasting insulin levels were measured. Homeostatic model assessment (HOMA) was used to quantify insulin resistance and beta-cell function. Genotyping (CDKAL1 and MTNR1B) performed using quantitative real-time TaqMan PCR.
7) Perez-Ferre et al[17] 2014	California (USA) RCT (2 Pprallel groups)	Baseline survey between January 2007 and December 2008 with 3 years of intervention and follow-up. 260 women (130 in the intervention group and 130 in the control group)	260 women with prior history of GDM (24 and 28 weeks of gestation with the Carpenter-Coustan criteria) who presented with normal FBS at 6-12 weeks postpartum. Exclusion criteria IFG (>100 mg/dL) in the first postpartum evaluation and plan for new pregnancy during the 3 years of follow-up.	Mediterrean lifestyle intervention (healthy mediterrean dietary intakes and improved physical activity).	Group 1 (n = 130) Mediterranean lifestyle intervention (educational program on nutrition and monitored physical activity program) group 2 (control, n = 130)—a conventional follow-up. Mediterranean diet pattern: -high consumption of fruits and vegetables (≥5 servings/day) -high consumption of legumes (≥2 servings/week) -high consumption of nuts (≥3 servings/week) -daily use of virgin olive oil (>40cc per day) - oily fish: at least 3 serving/ week) -low consumption of red and processed meats (<2 serving /week) -low consumption of non-skimmed dairy products (<2 serving/week) Physical exercise : warm-up exercise (10 minutes), aerobic activity; cycle-ergometer and treadmill exercise (15 minutes); muscular strengthening exercises with 2-3 sets of 8-10 repetitions for each muscular group (15 minutes); resting periods between the sets (10 minutes), and relaxation exercises (5 minutes).	-Follow-up OGTT 75 mg, HbA1c, HOMA-IR (at 12, 24, 36 months for both groups, additional 3, 6 months for interventional group) - A semi-quantitative questionnaire of food frequency and physical activity.	-Comparison of the effects of nutritional intervention with a monitored physical activity program and a standard follow-up on the prevention of glucose disorders (prediabetes/type 2 DM) 3 years after GDM development. -evaluation of the clinical changes and biochemical parameters in both groups, their adherence to lifestyle changes and predictive risk factors for conversion to glucose disorders in the postpartum period.

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Table 2. Characteristics of the Studies Included in Systematic Review (*Continued*)

First Author and Year of Publication	Country, Study Design	Time Frame, Number of Participants	Inclusion Criterion in Addition to History of GDM	Focus Area of Intervention	Primary Intervention	Assessments	Primary Outcome
8) Lee et al 2022[18]	Universiti Tunku Abdul Rahman, Kajang, Malaysia. RCT	January-December 2022. 130 women in the intervention group and 168 women in the control group	Women aged 20-49 years at baseline survey, and diagnosed with GDM Exclusion criteria: Chronic diseases, diabetes at the screening visit, medications known to alter OGTTs, planning to be pregnant in the next 2 years were excluded	Health educational intervention and Behavior change communication	For women in the intervention arm (n = 130), they received 1 session of individualized health education at 36 gestational weeks, a booklet of diabetes prevention, 5sessions of postpartum booster educational program which included 1 session of dietary and exercise counseling by dietician and physiotherapist at 6 weeks postpartum. For women in the control group (n = 168), standard treatment whereby they received group therapy on diet and physical activity modification by dietician and staff nurses during the antenatal period.	LDL, HDL, anthropometric measurements, blood pressure, glucose index, total cholesterol, triglyceride, incidence of type 2 diabetes mellitus (T2DM) 2 years after delivery by OGTT	LDL, HDL, anthropometric measurements, blood pressure, glucose index, total cholesterol, triglyceride, incidence of type 2 diabetes mellitus (T2DM) 2 years after delivery.
9) Tandon et al 2022 (RCT)[19]	19 urban hospitals in India, Sri Lanka, and Bangladesh.	They were enrolled from November 2017 to January 2020, and follow-up ended in January 2021. 1601 women randomized (800 women randomized to the intervention group and 801 women randomized to usual care)	Participants included women with a recent diagnosis of GDM who did not have type 2 diabetes at an oral glucose tolerance test (OGTT) 3-18 months postpartum.	A 12-month lifestyle intervention focused on diet and physical activity	A 12-month lifestyle intervention focused on diet and physical activity involving group and individual sessions, as well as remote engagement, adapted to local context and resources. This was compared with usual care.	The primary outcome was worsening category of glycemia based on OGTT using American Diabetes Association criteria: (1) normal glucose tolerance to prediabetes (i.e., impaired fasting glucose or impaired glucose tolerance) or type 2 diabetes or (2) prediabetes to type 2 diabetes.	The primary analysis consisted of a survival analysis of time to change in glycemic status at or prior to the final patient visit, which occurred at varying times after 12 months for each patient. Secondary outcomes included new-onset type 2 diabetes and change in body weight.

Table 3. Results and Conclusion from the Included Studies (n = 9)

Studies	Results	Conclusion from the Study
1) Gunderson et al[11]—2012	At 95% CI, the mean group difference fasting plasma glucose (mg/dL) Exclusive BF vs. Exclusive or mostly FF: −4.3 (−7.4 to −1.3) Mostly BF vs. Exclusive or mostly FF: −5.0 (−8.5 to −1.4) fasting insulin (mU/mL) Exclusive BF vs. Exclusive or mostly FF: −6.3 (−10.1 to −2.4) Mostly BF vs. Exclusive or mostly FF: −7.5 (−11.9 to −3.0) 2-hours insulin (mU/mL) Exclusive BF vs. Exclusive or mostly FF: −21.4 (−41.0 to −1.7) Mostly BF vs. Exclusive or mostly FF: −36.5 (−59.3 to −13.7) *P* < .05 (significant) for all the above. **Exclusive or mostly breastfeeding groups had lower prevalence of diabetes or pre-diabetes (*P* = .02).**	**Higher intensity of lactation** was significantly associated with improved fasting glucose and lower insulin levels at 6-9 weeks postpartum. **Lactation** may have **favorable effects** on glucose metabolism and insulin sensitivity that may **reduce diabetes risk after GDM** in pregnancy.
2) Zeigler et al[12]—2012	Data available—264 women. {201 (76%) breastfed their child, and 109 breastfed for 3 months} Full breastfeeding was practiced by 62%. Duration of lactation was inversely associated with postpartum diabetes risk (*P* = .002) women who breastfed for >3 months had the lowest postpartum diabetes risk (15-year risk: 42% [95% CI 28.9-55.1] no or ≤3 months of breastfeeding, 72% [60.5-84.7]; *P* = .0002) and a longer diabetes-free duration (18.2 years [95% CI 10.4-25.9]	**Breastfeeding** offers **a safe and feasible low-cost intervention** to reduce the risk of subsequent diabetes in this high-risk population.
3) Aroda et al[13]—2014	The incidence of diabetes was 11.4/100 person-years for women with a history of GDM compared with 6.9/100 person-years for women without a history of GDM among placebo participants. (48% higher risk of developing diabetes) with a history of GDM, ILS and metformin compared with placebo, reduced progression to diabetes by 35% and 40%, respectively. Without a history of GDM, ILS reduced the progression to diabetes by 30%, and metformin did not reduce the progression to diabetes	Both **ILS and metformin** were highly effective in **reducing progression** to diabetes during a 10-year follow-up period. Among women without a history of GDM, lifestyle but not metformin reduced progression to diabetes.
4) Hummel et al[14] —2017	At the end of the study, 9 diabetic events and 28 IFG/IGT events had occurred. Fifty-two women withdrew before the completion of the treatment phase. Because of the low diabetes rate, the study was terminated. Lifestyle adherence was similar in both the groups. At 24 months, the cumulative probability (in the placebo and Vildagliptin groups respectively) of; Postpartum diabetes was 3% and 5% (hazard ratio: 1.03; 95% CI : 0.15-7.36) IFG/IGT was 43% and 22% (hazard ratio: 0.55; 95% CI: 0.26-1.19)	In terms of reducing the risk of postpartum diabetes, the study **did not show** any significant **superiority of vildagliptin** over placebo. However, treatment was observed to be safe and suggested **some improvements in glycemic control, insulin resistance, and beta-cell function.**
5) Mirella Youssef Tawfik[15]—2016	After the intervention, percentage of women who had higher knowledge and belief scores had significantly increased from < 50% to ≥ 70 % in the intervention group (*P* < 0.001). More women in the intervention group reported the practice of exclusive breast feeding (85.4%) and screening for T2DM (43.7%) at 6 weeks postpartum compared to the control group (63.3 and 19.4% respectively) (*P* < 0.001). More women with excessive BMI in the intervention group (65 %) compared to the control group (11.6 %) were meeting the recommended Gestational Weight Gain (*P* < .001), and the postpartum weight (37.7 and 20.3% respectively) (*P* < .01).	**Health educational intervention—based on health belief model (HBM)** significantly **improved** the knowledge, beliefs, self-reported practices, and gestational & postpartum weight in patients with GDM, which will prevent the risk of developing type 2 DM.
6) Zhaoxia Liang et al[16]—2019	There was significant interaction between CDKAL1 and lifestyle intervention on changes in fasting insulin and HOMA-IR at 1 year (*P* = .008 and .006 respectively). The interactions between the CDKAL1 genetic variant and lifestyle intervention on changes in fasting insulin (*P* = .035) and HOMA-IR (*P* = .024) remained significant over the 2-year period, even though the effects of lifestyle intervention were attenuated at 2-year.	Women with the prior **GDM** (with the predisposing **CDKAL1** genetic variant) had improvement in **insulin resistance** with **healthy lifestyle intervention**.

(*Continued*)

Table 3. Results and Conclusion from the Included Studies (n = 9) (*Continued*)

Studies	Results	Conclusion from the Study
7) Perez-Ferre et al[17]—2014	Only 42.8% of the women in the intervention group (42.8%) developed glucose disorders, compared with the control group (56.75%, $P < .05$) after a 3-year follow-up period. The multivariate analysis showed a reduction in the rate of glucose disorders with a BMI < 27 kg/m^2 (OR 0.28, $P < .003$), low fat intake food pattern (OR 0.30, $P < .005$), low saturated fat food pattern (OR 0.30, $P < .005$), and healthy fat food pattern (OR 0.34, $P < .04$).	**Mediterrean Lifestyle intervention** was effective for the prevention of glucose disorders in women with prior GDM. Body weight gain and an unhealthy fat intake pattern were the most predictive factors for the development of glucose disorders in the postpartum period.
8) Lee et al—2022[18] (RCT)	There were no significant differences in baseline characteristics between groups for most of the variables examined except for educational level, in which the control group had a higher education than the intervention group. The women assigned to the system-based intervention showed significant differences to GDM women who were assigned to the control group for LDL and HDL, but not in anthropometric measurements, blood pressure, glucose index, total cholesterol, and triglyceride. In addition, it was found that the incidence of type 2 diabetes mellitus (T2DM) 2 years after delivery was 20% in the intervention arm compared to 17% in the control arm.	The system-based intervention was not statistically superior to the control intervention as there was no difference in the incidence of T2DM between the intervention and control groups. We, therefore, suggest that more intensive interventions are needed to prevent GDM from developing into T2DM.
9) Tandon et al—2022[19] (RCT)	A total of 1823 women (baseline mean [SD] age, 30.9 [4.9] years and mean [SD] body mass index, 26.6 [4.6]) underwent OGTT at a median (IQR) 6.5 (4.8-8.2) months postpartum. After excluding 160 women (8.8%) with type 2 diabetes, 2 women (0.1%) who met other exclusion criteria, and 49 women (2.7%) who did not consent or were uncontactable, 1612 women were randomized. Subsequently, 11 randomized participants were identified as ineligible and excluded from the primary analysis, leaving 1601 women randomized (800 women randomized to the intervention group and 801 women randomized to usual care). These included 600 women (37.5%) with prediabetes and 1001 women (62.5%) with normoglycemia. Among participants randomized to the intervention, 644 women (80.5%) received all program content, although COVID-19 lockdowns impacted the delivery model (i.e., among 644 participants who engaged in all group sessions, 476 women [73.9%] received some or all content through individual engagement, and 315 women [48.9%] received some or all content remotely). After a median (IQR) 14.1 (11.4-20.1) months of follow-up, 1308 participants (81.2%) had primary outcome data. The intervention, compared with usual care, did not reduce worsening glycemic status (204 women [25.5%] vs. 217 women [27.1%]; hazard ratio, 0.92; [95% CI, 0.76-1.12]; $P = .42$) or improve any secondary outcome.	This study found that a large proportion of women in South Asian urban settings developed dysglycemia soon after a GDM-affected pregnancy and that a lifestyle intervention, modified owing to the COVID-19 pandemic, did not prevent subsequent glycemic deterioration. These findings suggest that alternate or additional approaches are needed, especially among high-risk individuals.

Data Availability Statement: The data that support the findings of this study are within the manuscript.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – A.M., K.S.; Design – A.M., R.R.; Supervision – A.M., P.G.; Resources – K.S., A.P.; Materials – P.G., A.P.; Data Collection and/or Processing – A.M., K.S.; Analysis and/or Interpretation – A.M., K.S.; Literature Search – A.M., K.S.; Writing – A.M., R.R.; Critical Review – R.R., A.P.

Declaration of Interests: The authors have no conflicts of interest to declare.

Funding: This study received no funding.

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