Associations between plant-based diets, plant foods and botanical supplements with gestational diabetes mellitus: a systematic review protocol

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ABSTRACT

Introduction  Gestational diabetes mellitus (GDM) is one of the most common health complications during pregnancy. Medical nutrition therapy is the mainstay of treatment for GDM, however, there is no current consensus on optimal dietary approaches to prevent or control hyperglycaemia in pregnancy. The aim of this systematic review is to assess the relationships between plant-based dietary patterns, plant foods and botanical dietary supplements with GDM and maternal glycaemic biomarkers.

Methods and analysis  A predefined search strategy was used on 16 June 2021, to search PubMed, Embase and CINAHL Plus with Full Text (EBSCOhost), as well as ClinicalTrials.gov, for studies published as original articles in English. Articles will be included if they are human observational studies or clinical trials and will be excluded if they are review articles or conference abstracts. We will use Cochrane’s risk of bias tools for interventions that are parallel arm (Risk of Bias tool for randomised trials version 2 (RoB 2)) and single arm, non-randomised intervention studies (Risk of Bias In Non-randomised Studies-of Interventions (ROBINS-I)). For observational, case–control and cross-sectional studies, we will use the National Heart, Lung and Blood Institute’s quality assessment tools. Data will be synthesised in a narrative format describing significant results as well as presenting the results of the quality assessment of studies.

Ethics and dissemination  This systematic review does not require ethical approval as primary data will not be collected. The review will be published in a peer-reviewed journal and disseminated electronically and in print.

PROSPERO registration number  CRD42022306915.

INTRODUCTION

Gestational diabetes mellitus (GDM) is a metabolic disorder characterised by hyperglycaemia first identified during pregnancy and is one of the most common health complications during gestation.1–4 Depending on the criteria used to diagnose GDM, prevalence estimates range between 2% and 10% in the USA, roughly 16% worldwide and as high as 38% in Southeast Asian countries.5–7 GDM can cause detrimental short-term and long-term health outcomes for both the pregnant individual and neonate. For pregnant individuals, there is an increased risk for delivery complications including stillbirth,8 future risk of type 2 diabetes (T2D)9 and cardiovascular disease.10 For the child, risks include macrosomia,11 low and high birth weight,10 and future risk of T2D and obesity when compared with children born to non-GDM pregnancies.12–16

Common risk factors of GDM include prepregnancy overweight (body mass index (BMI) 25.0–29.9 kg/m²) or obesity (BMI ≥30.0 kg/m²), older maternal age, history of diabetes, a first-degree family history of T2D or GDM, and having a racial identity that is non-white.1–16 It has been reported that at least 70% of women diagnosed with GDM, using the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criterion, are able to manage hyperglycaemia with lifestyle modifications including adhering to medical nutrition therapy (MNT), weight management and increasing physical activity.17 18 The standard of care is to provide MNT as the primary strategy for managing
GDM prior to pharmaceutical intervention. However, there is limited evidence and consensus on best practice dietary approaches for optimising glucose levels in GDM, and for preventing GDM in at-risk pregnancies.

Several studies show that maternal diets low in fibre and high in glycaemic load increase risk of GDM. A systematic review of 21 studies (83,189 women, 478 with GDM) by Schoenaker et al. concluded that prepregnancy and during pregnancy dietary patterns rich in fruits, vegetables, whole grains and fish, and low in red meats, refined grains, and high-fat dairy are beneficial in decreasing risk of GDM. Whereas higher intake of cholesterol, total fat, heme iron, and foods like eggs, red meats and processed meats are associated with higher risk of GDM. Moreover, plant-based diets, like the Mediterranean Diet, which is high in antioxidants, micronutrients, fibre and phytochemicals is associated with reduced risk of GDM.

A narrative review by Pistollato et al. examined the protective effects and potential shortcomings of plant-based diets during pregnancy as it relates to health risks, including GDM. However, the authors only discussed the protective effects of dietary fibre and the Dietary Approaches to Stop Hypertension (DASH) diet in preventing and managing GDM (results were from one prospective cohort study and one randomized controlled trial, (RCT)). Results from this review showed that 10 g/day of fibre was associated with a 26% reduction in risk of GDM, and that individuals following the DASH diet underwent fewer caesarean sections and fewer required insulin therapy after the intervention. Additionally, a systematic review by Raghavan et al. examined dietary patterns before and during pregnancy and risk of maternal outcomes, including GDM. The authors found that dietary patterns higher in fruits, vegetables, whole grains, nuts, legumes and fish and lower in red and processed meats consumed before pregnancy were associated with a lower risk of GDM in 8 out of 11 of the studies reviewed. Although their results support plant-based dietary patterns in GDM prevention, the focus included non-plant-based dietary patterns and lacked specific focus on plant foods or botanical supplements. Similarly, a descriptive review by Schiattarella et al. examined associations between plant-based diets and GDM and concluded that plant-based diets may reduce the onset of GDM. However, this review only assessed observational studies, lacked a systematic approach, inclusion of clinical trials, and examination of specific plant foods, and botanical dietary supplements.

While these published reviews examined maternal diet and associations with GDM, no study systematically reviewed the specific role of plant-based diets, plant foods and botanical dietary supplements for GDM prevention and control. Therefore, the aim of this systematic review is to comprehensively examine the relationship between plant-based diets, plant foods and botanical dietary supplements in the (1) prevention and management of GDM and (2) maternal glycaemia in observational studies and clinical trials.

**METHODS AND ANALYSIS**

**Study design**

The protocol includes all relevant PRISMA-P checklist items (see in online supplemental file 1) related to the objectives of this review.

**Patient and public involvement**

The study design protocol does not involve patient recruitment or public involvement.

**Inclusion criteria**

The Patient, Intervention/exposure, Comparison, Outcome, Study Design criteria format was used to guide the inclusion criteria parameters (table 1). Studies will be included if they are (1) human studies with pregnant individuals or soon to be pregnant who have GDM or are at risk for developing GDM; (2) are either observational or intervention studies examining intake of plant-based diets, plant foods or botanical dietary supplements and (3) are examining the incidence of GDM or maternal glycaemic markers as an outcome. For the purposes of this systematic review, only original research articles, in English, will be considered.

The exposures or interventions examined for this systematic review consist of plant-based diets, plant foods and botanical dietary supplementation in humans as it relates to GDM and maternal glycaemic outcomes. These three broad diet categories are as follows: (1) Plant-based diets includes dietary patterns that largely contain plant-based food items, and where animal foods and products are limited. This will include diets like a vegan,

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<th>Table 1</th>
<th>PICOS criteria for study inclusion</th>
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<td><strong>Parameter</strong></td>
<td><strong>Inclusion criteria</strong></td>
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<tr>
<td><strong>Population</strong></td>
<td>Women who are pregnant or become pregnant that are at risk for or diagnosed with GDM</td>
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<td><strong>Intervention/exposure</strong></td>
<td>Dietary interventions or observational studies involving plant-based dietary components</td>
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<td><strong>Comparison</strong></td>
<td>Partial or total exclusion of plant-based dietary components or an alternative diet or placebo</td>
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<td><strong>Outcome</strong></td>
<td>GDM incidence and maternal glycaemic markers</td>
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<tr>
<td><strong>Study design</strong></td>
<td>Human observational or clinical trials</td>
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GDM, gestational diabetes mellitus; PICOS, Patient, Intervention, Comparison, Outcome, Study Design.
vegetarian, Mediterranean and DASH. (2) Plant foods, including plant-based components, such as fruits, vegetables, grains, legumes, like soy, nuts and seeds, dietary fibre and dietary vegetable protein. (3) Botanical supplements such as curcumin, supplemental fibre and vegetable protein will be included.

Outcomes will include GDM diagnosis and maternal glycaemic markers. GDM diagnosis will be based on the guidelines provided by the American Diabetes Association, IADPSG, WHO or any other hospital-based criteria. Maternal glycaemic markers will be based on screening tests for glucose and insulin. Tests for glucose will include fasting plasma glucose, fasting blood glucose (FBG), oral glucose tolerance test and haemoglobin A1c (HbA1c). Tests for insulin will include, but are not limited to, Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) and Homeostasis Model Assessment of β-cell function (HOMA-B).

Exclusion criteria

Papers will be excluded from this systematic review if they are: (1) studies performed in animals or cells/in vitro (experimental studies); (2) review articles or conference abstracts or abstract only papers (3); publications where non-pregnant individuals are examined; (4) publications where pregnant individuals without GDM diagnosis or maternal glucose markers are examined; (5) publications where plant-based diets, plant foods or botanical supplements are not examined; (6) publications where the study does not examine the effect or associations among plant-based diet, plant foods or botanical supplements with GDM or glucose markers; (7) papers published in a language other than English (8) publications where single or multiple micronutrients are examined (i.e., vitamins, minerals).

Information sources and search strategy

Using an a priori research protocol (PROSPERO registration number CRD42022306915), designed with a health sciences librarian (RH), relevant articles were identified on 16 June 2021 from PubMed, Embase and CINAHL Plus with Full Text (EBSCOhost), and ClinicalTrials.gov. A search strategy, including keywords, for these databases is provided in (online supplemental file 2). RH created a text file with all articles for screening. This text file was converted to an Excel file that contains titles, author, abstract, journal and publishing date. Unpublished clinical trials will be manually searched using two databases, bioRxiv (https://www.biorxiv.org/) and NIH Reporter (https://reporter.nih.gov/), to identify additional articles. If we are unable to find published data for a registered trial, we will contact the principal investigator via email to determine the status of the trial. Additionally, on completion of the full text screening, RH will perform the same search and a forward search to include recent publications after 16 June 2021. Any studies that fit our inclusion criteria will be added to this review.

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<th>Table 2</th>
<th>Preliminary data extraction instrument</th>
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<td><strong>Intervention studies</strong></td>
<td><strong>Observational studies</strong></td>
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<tr>
<td>Author, year, country</td>
<td>Author, year, country</td>
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<td>Intervention design (eg, double blinded RCT, type (eg, feeding trial) and duration)</td>
<td>Study design (eg, cross-sectional, case-control) and duration</td>
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<td>GDM diagnosis criteria used</td>
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<td>Significant findings</td>
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BMI, body mass index; GDM, gestational diabetes mellitus; RCT, randomized controlled trial.

Study selection

Three reviewers from four total reviewers (JU, KC, BD and HJ) will independently screen each title, abstract and full text article for inclusion. At each phase, disputes will be discussed at weekly meetings with the authorship team to reach consensus. Full-text articles that do not meet the inclusion criteria will be excluded and reasons for exclusion will be documented. Reference lists of included articles will be hand searched for additional articles, which will then be assessed using the same eligibility criteria and screening process as described above.

Data extraction

A predefined data extraction criteria developed by the research team will be utilised (table 2). Three of four reviewers (KC, BD, HJ and JU) will independently extract data from each full text article selected for inclusion. Any disputes during data extraction, including removal or addition of information, will be discussed in full authorship meetings for consensus. The extracted data will include the following: author, year of publication, country, study design, sample size, mean age, mean BMI, ethnicity/race, intervention/exposure, study duration, dietary assessment method, GDM diagnosis criteria and outcomes including maternal glycaemic measures such as FBG, oral glucose tolerance, HbA1c, HOMA-IR and HOMA-B.

Risk of bias and quality assessment tools

Risks of bias within clinical trials and quality assessment for observational studies will be independently examined by two authors from a total of six reviewers (JU, TCJB, MDK, HJ, KC and BD). For parallel arm, randomised intervention studies, the Cochrane Handbook for Systematic
Reviews of Interventions, Risk of Bias tool version 2 (RoB 2) will be used. Components of the Cochrane tool include scoring biases based on six domains: 1) bias arising from the randomisation process, 2) bias due to deviations from intended interventions, 3) bias due to missing outcome data, 4) bias in measurement of the outcome and 5) bias in selection of the reported result. For single arm, non-randomised intervention studies, Cochrane’s Risk of Bias In Non-Randomised Studies-of Interventions, ROBINS-I, tool will be used. Components of the ROBINS-I tool include scoring biases based on seven domains: 1) bias due to confounding, 2) bias in selection of participants into the study, 3) bias in classification of interventions, 4) bias due to deviations from intended interventions, 5) bias due to missing data, 6) bias in measurement of outcomes and 7) bias in selection of the reported result.

Quality of observational studies will be assessed using the National Heart, Lung and Blood Institute (NHLBI) Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies and the Quality Assessment of Case-Control Studies. These tools are designed to support the reviewers in determining the internal validity of each study using either a 12 (for case-control studies) or a 14 question (for cohort and cross-sectional studies) guide to rate studies as ‘good’, ‘fair’ or ‘poor’ quality. After independently rating each study, reviewers will discuss any differences in their scoring and judgements and resolve disagreements collectively at the author meetings. Examples of these tools are shown online in (online supplemental file 3).

Data synthesis
According to the expected heterogeneity of studies included in this review, a narrative synthesis will be carried out, focusing on the study types and the outcomes of interest. The findings and quality of each study, using the Cochrane and NHLBI platforms, will be presented in summary tables. We will narratively summarise results by describing significant associations as increase, decrease or no difference in both observational studies and clinical trials for GDM risk and the glycaemic markers. When available, odds or risk ratios may be used to compare differences based on the type of plant-based diets, plant foods and botanical supplements as an exposure or intervention. Additionally, for clinical trials, we may compare mean differences in GDM incidence and changes in maternal glycaemic markers between control versus intervention groups. We expect to identify differences in reporting associations across studies including examining tertiles, quartiles or quintiles for adhering to a specific plant-based dietary components, thus our data synthesis will remain narrative in nature.

ETHICS AND DISSEMINATION
This systematic review does not require ethical approval as primary data will not be collected. This review will be published in a peer-reviewed journal and disseminated electronically and in print.

DISCUSSION
This systematic review will provide a comprehensive summary of the role of plant-based diets, plant foods and botanical supplements for GDM prevention and control. Given as many as 16% of pregnant individuals worldwide are afflicted by GDM, findings from this review can inform future clinical trials and clinical recommendations for GDM prevention and management. Additionally, providing easy-to-implement dietary modifications for pregnant individuals can improve maternal and child health, and therefore, reduce healthcare costs and burden.

Key strengths of this study include the comprehensive systematic search to identify GDM prevention and treatment studies that will provide a broad understanding of the relationship between plant-based dietary components and GDM and maternal glycaemic markers. However, a methodological limitation of this systematic review is the exclusion of abstracts and non-English language publications. Another limitation of this study is that our definition of ‘plant-based diet’ includes foods of animal origin, such as fish in the case of the Mediterranean diet. Therefore, we are not exclusively analysing diets where only plant-based foods are consumed.

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Contributors TCJB led the concept of this project and research questions with contributions from LT-H, JM and BM. TCJB and JU developed and submitted the research protocol and determined the eligibility criteria with assistance from LT-H, RH, KC, HJ and BD. RH developed the search strategy and performed the search. TCJB, JU, KC, HJ and BD performed the screening. JU, KC, HJ and BD performed the quality assessment. JU and TCJB drafted this protocol manuscript and will draft the final manuscript. TCJB, JU and LT-H revised this protocol manuscript and will revise the final manuscript. TCJB and LT-H provided oversight for the project. All authors read and approved the final version of this protocol manuscript.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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REFERENCES


13 ACOG. [Internet]. Gestational Diabetes - ACOG. 2017 Available: www.acog.org/Patients/FAQs/Gestational-Diabetes?IsMobileSet=false


27 Schiattarella A, Lombardo M, Moriando M, et al. (4), available from. Antioxidants (Basel) [Internet]


