DIABETES AND PREGNANCY (M-F HIVERT AND CE POWE, SECTION EDITORS)

Evidenced-Based Nutrition for Gestational Diabetes Mellitus

Amita Mahajan¹ · Lois E. Donovan² · Rachelle Vallee³ · Jennifer M. Yamamoto^{2,4}

Published online: 31 August 2019 © Springer Science+Business Media, LLC, part of Springer Nature 2019

Abstract



Purpose of Review To review the latest evidence for dietary interventions for treatment of gestational diabetes (GDM). **Recent Findings** High-quality systematic reviews demonstrate no major advantages between the low-carbohydrate or calorierestricted diets. However, the low glycemic index (GI) diet, characterized by intake of high-quality, complex carbohydrates, demonstrated lower insulin use and reduced risk of macrosomia in multiple reviews. Recent evidence suggests the Mediterranean diet is safe in pregnancy, though trials are needed to determine its efficacy over conventional dietary advice. Currently, there are insufficient data to support the safety of the ketogenic diet for the treatment of GDM.

Summary The low GI diet may improve maternal and neonatal outcomes in GDM. The liberalized carbohydrate intake is less restrictive, culturally adaptable, and may improve long-term maternal adherence. Further research is needed to establish the optimal, most sustainable, and most acceptable medical nutrition therapy for management of women with GDM.

Keywords Gestational diabetes \cdot Medical nutrition therapy \cdot Ketogenic diet \cdot Low-carbohydrate diet \cdot Low glycemic index diet \cdot Pregnancy

Introduction

Gestational diabetes mellitus (GDM) is one of the most common medical disorders of pregnancy, affecting up to 18% of all pregnancies [1]. It is associated with an increased risk of adverse pregnancy outcomes for both mothers and their offspring [1–4]. Parallel to the rise in obesity and type 2 diabetes, the prevalence of GDM has risen steadily over the past 50 years [5]. In 2014, the estimated number of obese or overweight pregnant women was nearly 40 million [6]. The overall population attributable factor of overweight/obesity to GDM is 46.4%, meaning nearly half the GDM cases are potentially preventable if women had pre-pregnancy BMIs of $< 25 \text{ kg/m}^2$ [7].

The GDM diagnostic criteria cut-off values are based on the risk of adverse pregnancy outcomes, with a continuum of risk appreciated with worsening maternal glucose control [8-10]. For offspring, the adverse effects of GDM extend beyond increased birth weight and large for gestational age (LGA) to include neonatal hypoglycemia, neonatal adiposity, jaundice, and birth trauma [3, 9]. The maternal impact of GDM is seen in the increased risk of preeclampsia, number

This article is part of the Topical Collection on Diabetes and Pregnancy

Jennifer M. Yamamoto jennifer.yamamoto@ucalgary.ca

> Amita Mahajan Amita.Mahajan@albertahealthservices.ca

Lois E. Donovan Lois.Donovan@albertahealthservices.ca

Rachelle Vallee Rachelle.Vallee@albertahealthservices.ca

- ¹ Department of Medicine Division of Endocrinology and Metabolism, Cumming School of Medicine, University of Calgary, Calgary, Canada
- ² Department of Medicine Division of Endocrinology and Metabolism, Department of Obstetrics and Gynecology, and Alberta Children's Hospital Research Institute Calgary, Cumming School of Medicine - University of Calgary, Calgary, Canada
- ³ Diabetes in Pregnancy Clinic, Alberta Health Services, Calgary, Canada
- ⁴ Cumming School of Medicine, Richmond Road Diagnostic and Treatment Centre, University of Calgary, 1820 Richmond Road SW, Calgary, AB T2T 5C7, Canada

of cesarean sections, and perineal trauma [3, 11]. Importantly, women with GDM reportedly have a sevenfold increased risk for developing type 2 diabetes postpartum, with many diagnosed within only a few years postpartum [12].

The current first-line therapy for GDM is medical nutrition therapy with the addition of insulin and/or oral anti-hyperglycemic agents if glycemic targets are not achieved with diet and lifestyle alone [4]. Nutrition therapy is particularly important as it is applicable to management of all women with GDM, regardless of their phenotypic severity. Adequate nutrition therapy should promote intake of high-quality ingredients, appropriate gestational weight gain without over-nutrition, and adequate fetal growth [4, 13]. Effective treatment of GDM results in improved perinatal outcomes including decreased risk of preeclampsia, macrosomia, and shoulder dystocia [14, 15]. Importantly, approximately 70% of women can control GDM with lifestyle and nutrition alone, highlighting the importance of evidence-based diet recommendations [4].

Despite the incidence of GDM and the established importance of medical nutrition therapy, the optimal diet for GDM remains elusive. Recent systematic reviews examining nutrition therapy in GDM suggest there may be room for improvement in our current guideline recommendations which are focused on controlling carbohydrate intake, without much guidance on other nutritional aspects—for example, other macronutrient intake, quality of the nutrient choices (carbohydrates and others), and/or dietary patterns. The purpose of our review is to evaluate current recommendations for GDM nutrition management and their supporting evidence, review common and uncommon proposed GDM diets, and ultimately to provide evidenced-based recommendations for optimal medical nutrition therapy for this increasing number of mothers.

Current Treatment Recommendations

The Endocrine Society recommends all women with GDM are managed with medical nutrition therapy, physical activity, weight management, and glucose monitoring [13]. Medical nutrition therapy is defined as "*a carbohydrate controlled meal plan that promotes adequate nutrition with appropriate weight gain, normoglycemia and the absence of ketosis*" [13]. It should be implemented as an individualized nutrition plan under the care of a registered dietitian familiar with GDM and should highlight healthy food choices, portion control, and preparing foods at home while considering individual patient factors (i.e., personal or cultural preferences, socioeconomic status, physical activity etc.) [4, 13].

Based on the Dietary Reference Intake, to meet the average daily nutrient requirements, all pregnant women should consume a minimum of 175 g of carbohydrates, 71 g of protein, and 28 g of fiber per day [4]. A moderate energy restriction (1600–1800 kcal/day) is suggested only for overweight/obese

women with GDM as a means of improving maternal glycemia without impacting fetal growth or inducing significant maternal ketosis [13, 16]. The Endocrine Society suggests limiting carbohydrates to 35–45% of total daily calories, distributed evenly throughout the day [13]. However, there is significant guideline variability globally for the recommended carbohydrate intake, ranging from 26 to 60% carbohydrate of daily caloric intake, with not all guidelines advocating women chose carbohydrates with a low glycemic index (GI) when possible [17•, 18]. Table 1 summarizes major national guideline recommendations for medical nutrition therapy in GDM.

Limitations of Current Recommendations

Presently, there is no particular diet recommended for GDM; however, controlling carbohydrate intake (particularly simple carbohydrates) has been traditionally favored as it blunts postprandial hyperglycemia [22]. Despite its widespread recommendation, large reviews have found carbohydrate-restricted diets lack highquality evidence [1, 17•, 23, 24], have poor adherence due to their restrictive nature [25], and may have unintended harmful consequences from replacement of carbohydrate calories with fat [22]. Low-carbohydrate diets are typically low in fiber which can exacerbate the existing concerns of constipation in pregnancy, another feature that may impair ongoing adherence [26, 27]. Perhaps most importantly, some women find the restrictive carbohydrate-controlled diet difficult to adopt and sustain long term [28]. Women report fear of losing control of GDM during diet management [28] and challenges with rapid need for diet change, as well as complete mental exhaustion surrounding restrictive food choices [29]. Nutrition therapy focused on restricting carbohydrates fosters maternal anxiety [25] and has been described by many women as culturally unacceptable, an important factor that undermines nutrition therapy in GDM on a global level [22].

Evidence is mounting to suggest our current medical nutrition guidelines have room for some sustainable and patientcentered amendments. A recent systematic review and metaanalysis of 18 studies (n = 1151) found modified dietary interventions beyond the usual dietary advice for GDM resulted in improved maternal glycemic control and infant birth weight outcomes [17•]. A post hoc analysis revealed significant heterogeneity between countries when comparing the composition of the diets used by the control groups in trials assessing modified dietary interventions [18]. Although the optimal diet for GDM is still debatable, identifying contributing or therapeutically efficacious components that abate the need for medical therapy, while optimizing maternal and neonatal outcomes, is imperative for effective and sustainable management of this increasing population of mothers [22].

Page 3 of 10 94

Table 1 Summary of current national guideline recommendations for medical nutrition therapy in gestational diabetes		Recommendations	
	American Diabetes Association [4]	An individualized nutrition plan should be developed between the women and a registered dietitian familiar with GDM management. Food plan should be based on the recommended dietary reference intake for all pregnant women: 175 g of carbohydrate, a minimum of 71 g of protein, and 28 g of fiber per day.	
		The amount and type of carbohydrate will impact postprandial glycemia, but specific calorie or carbohydrate amounts are not provided.	
	Diabetes Canada [19]	Refer all women for assessment, counseling, and follow-up by registered dietitian at diagnosis of gestational diabetes. Nutrition therapy should emphasize a healthy diet with a minimum of 175 g/day of carbohydrates, distributed over 3 moderated-sized meals and 2 or more snacks (one at bedtime), as well as replace high GI foods with low GI foods.	
	Endocrine Society [13]	Limit carbohydrate intake to 35–45% of total calories, distributed in 3 small- to moderate-sized meals and 2–4 snacks including an evening snack. Glycemic control is influenced by restricting total carbohydrate intake, distributing amounts of carbohydrate over several meals and snacks, and choosing higher quality and lower GI foods.	
		Moderate caloric restriction (1600–1800 kcal/day or 33% reduction in total calories) is appropriate for overweight or obese women with GDM.	
	National Institute for Health and Care Excellence (NICE) Guidelines [20]	Refer all women to a registered dietitian at time of diagnosis of gestational diabetes. Advise women to follow a healthy diet in pregnancy, emphasizing that foods with a low GI should replace those with a high GI.	
	International Diabetes Federation (IDF) [21]	An individualized and culturally sensitive nutrition plan should be provided by a healthcare professional with expertise in GDM medical nutrition therapy. Women should have the type, quality, and quantity of carbohydrate food matched to insulin type and dosage. Glycemic control is influenced by regulating total carbohydrate intake, the proportion of carbohydrate consumed, and by following a low GI diet.	
		Moderate energy reduction of no more than 30% of habitual caloric intake is safe for women with GDM who are considerably overweight (no BMI specified).	

GDM gestational diabetes mellitus, GI glycemic index, BMI body mass index

Low-Carbohydrate Diet

Definition

A low-carbohydrate diet is defined as intake from carbohydrates consisting of < 35-45% of total daily energy intake or <130 g of carbohydrate per day for a non-pregnant woman [30, 31].

Supporting Evidence

In GDM, restriction of simple carbohydrates has been shown to reduce postprandial hyperglycemia, fetal glucose exposure, and fetal overgrowth [31, 32]. Nearly 30 years ago, Peterson et al. measured the glucose response to various proportions of carbohydrates in women with GDM not requiring insulin.

Investigators measured 1-h postprandial glucose values to meals with varying carbohydrate proportions. To meet the recommended 1-h target of < 7.8 mmol/L, the following percentage of calories from carbohydrates per meal was required: 45% at breakfast, 55% at lunch, and 50% at dinner. Peterson et al. noted the glycemic response to mixed meals, which contained a consistent proportion of fat and protein, was predominantly correlated with the proportion of carbohydrate consumed [33]. This finding contributed to the focus on carbohydrate intake in GDM and was corroborated when Major and colleagues reported an association between postprandial hyperglycemia and infant size in 1998 [34]. These investigators conducted a non-randomized study of women with GDM and demonstrated target glycemic control may be achieved through diet. They discovered consumption of <42% carbohydrate/day may avoid the need for insulin during pregnancy, lower postprandial glucose, and reduce the risk of LGA, macrosomia, and cesarean-section [34].

Opposing Evidence

In contrast, these findings have not been reproduced in larger randomized studies or systematic reviews. Two small randomized trials of women with GDM (not on insulin) compared a low-carbohydrate diet (40-45% carbohydrate of daily caloric intake) to a high-carbohydrate/control diet (55-65% carbohydrate of daily caloric intake). They found no significant differences in overall glycemic control, insulin use, or obstetrical and neonatal outcomes including maternal hypertension, preterm delivery, cesarean-section, LGA, or neonatal hypoglycemia [35, 36]. Hernandez et al. conducted a well-matched, randomized pilot clinical trial in which all meals were provided. Twelve overweight/obese women with GDM were randomized to either conventional low-carbohydrate/higher-fat diet (40% carbohydrate/45% fat/15% protein of daily caloric intake) or a higher-complex carbohydrate/lower-fat diet (60% carbohydrate/25% fat/15% protein of daily caloric intake). After 7 weeks, the higher carbohydrate-diet group had lower fasting glucose (p = 0.03), less insulin resistance (p = 0.005), reduced expression of pro-inflammatory genes (p < 0.01), and a trend towards lower serum free fatty acids (FFAs) (p = 0.06). Although this is a pilot study, the results challenge the current recommendations of carbohydrate limitation and demonstrate potential for improved glycemic control and metabolic parameters with a more liberalized carbohydrate intake. The key difference between the diets in this trial was the highcarbohydrate diet that contained more complex carbohydrates with lower glycemic indices, suggesting the type and quality of carbohydrate is paramount [37•].

In addition to Yamamoto et al., two systematic reviews and meta-analyses have compared the impact of various dietary interventions in GDM and have shown consistent results. Viana et al. reviewed nine randomized trials (n = 884) comparing the impact of low GI diets, low-carbohydrate diets, and energy-restricted diets on maternal and newborn outcomes in GDM. The authors found no difference in frequency of insulin use, number of cesarean-sections, or risk of macrosomia between low-carbohydrate diets (<45% carbohydrates of daily caloric intake) compared to control diets (55–60% carbohydrates of daily caloric intake) [24]. More recently, a Cochrane review from 2017 reviewed 19 trials (n = 1398) and found no clear benefit in maternal or neonatal outcomes between diets (including the currently recommended low-carbohydrate diet) [23].

In addition to fostering maternal anxiety, carbohydrate restriction can result in unbalanced macronutrient intake and potentially unintended harmful consequences on offspring. In efforts to adhere, women often replace their carbohydrate calories with an increase in fat, which often includes saturated and processed fats due to low cost and availability of these foods [22]. Normal adaptations of pregnancy physiology include amplified maternal insulin resistance and lipolysis to increase maternal FFA, amino acids, and glucose to ensure adequate nutrient shunting to the fetus [38]. A diet high in saturated and processed fats can increase maternal FFA and triglyceride production beyond typical requirements. This dampens insulin signaling augmenting the already amplified hepatic and peripheral maternal insulin resistance, leading to prolonged postprandial hyperglycemia [38]. This finding is supported by studies outside of pregnancy that demonstrate a high-fat, low-carbohydrate diet (< 20 g/day) can result in a blunted 24-h insulin secretion and worsening of insulin resistance [39]. The major concern with worsening maternal insulin resistance is the increase in substrates (i.e., FFA, triglycerides, etc.) available for shunting to the fetus stimulating fetal overgrowth and fat accretion [22]. There is emerging evidence that maternal triglycerides and FFAs may be additional contributors of fetal overgrowth and fetal fat accretion to maternal glucose [22, 40]. These potential unintended consequences should be considered when advocating for varying degrees of carbohydrate restriction in nutrition therapy for GDM.

Ketogenic Diet

Definition

A ketogenic diet is a variation of a very low-carbohydrate diet that is defined as < 20-50 g of carbohydrate per day or < 10% calories from carbohydrates per day. The remaining calories are replaced with more energetically dense fat and protein. These values are derived from the level of carbohydrate intake that is expected to produce ketosis in most adults [31].

Background

The ketogenic diet has recently gained popularity amid the general public, such that clinicians are frequently asked about its role in pregnancy, and particularly in the management of GDM. To our knowledge, a ketogenic diet has never been studied as primary nutrition therapy in women with GDM. Most evidence examining the effects of gestational ketosis are derived from animal studies or focus on the presence of ketones as a result of maternal malnutrition, prolonged fasting, or in the context of diabetic ketoacidosis (DKA). It is important to remember that ketones are not uncommon in pregnancy due to the many physiologic changes that occur in the face of increased metabolic demands and in effort to provide a constant supply of nutrients to the developing fetus [41, 42]. It is not clear whether pathological ketosis or mild gestational ketosis is different from the stable ketosis that occurs in ketogenic diets, which typically imply adequate caloric intake [41].

Diet	Definition	Potential benefits of diet	Potential drawbacks of diet
Low-carbohydrate diet	< 35–45% of daily caloric intake from carbohydrates OR < 130 g carbohydrates/day for non-pregnant woman [30, 31]	 ↓ postprandial hyperglycemia, ↓ fetal glucose exposure, and ↓ fetal overgrowth/LGA [31, 32] ↓ HbA1c and triglycerides outside of pregnancy [31] 	 Lack of high-quality evidence in GDM [1, 17•, 23, 24] Restrictive and anxiety provoking [25] Commonly low in fiber [26] Unintended consequences of increased maternal fat intake [22] Concerns with long-term adherence and sustainability [25, 26, 28]
Ketogenic diet	< 10% of daily caloric intake from carbohydrates OR < 20–50 g of carbohydrates/day [31]	 Improved glycemic control and ↓ number of diabetes medications outside of pregnancy [31] 	 Lack of short and long-term safety data in pregnancy in humans Neurodevelopmental concerns in animal models and human offspring [43, 46, 47] Unintended consequences of increased maternal fat intake [22]
Low GI diet	GI estimates the glucose response to intake of a carbohydrate food item; food items with a GI of < 55 are considered low GI foods [48].	 Improved glycemic control [49] ↓ postprandial hyperglycemia, ↑insulin sensitivity, ↓ overall insulin requirements, ↓ need for diabetes medications [31, 51, 52] Less restrictive [49] Added dietary fiber content mout further this participation (52) 	 No major safety concerns identified Cost and access to high-quality foods may limit adherence and applicability [57, 58]
Caloric restriction	Severe caloric restriction: total intake of <1500 kcal/day <u>OR</u> 50% reduction from pre-pregnancy caloric intake. Moderate caloric restriction: 1600-1800 kcal/day OR 30% reduction from pre-pregnancy intake [13].	 Improved glycemic control and weight loss outside of pregnancy [31] Improved glycemic control in overweight/obese women with GDM 	 No significant benefit in maternal or neonatal outcomes [17•, 23, 24] Risk of maternal ketosis [13, 59] Must be balanced with adequate gestational weight gain [60]
Mediterranean diet	High consumption of vegetables, fruit, nuts, seeds, legumes, olive oil, and unprocessed grains. Moderate intake of fish and poultry and limited consumption of dairy products, red meat, processed meats, or refined sugars [62, 63].	 Beneficial effects on overall cardiovascular health, risk of diabetes, and obesity outside of pregnancy [62, 64, 65] Evidence of safety in pregnancy [63] 	 No major concerns identified, but may have similar concerns with cost and access to high-quality foods limiting adherence and applicability Randomized control trial needed to determine efficacy as a nutrition therapy for GDM [63]

 Table 2
 Summary of diets for medical nutrition therapy in gestational diabetes

GI glycemic index, HbA1c hemoglobin A1c, LGA large for gestational age

Supporting Evidence

The benefits of a ketogenic diet in diabetes from nonpregnancy studies include improved hemoglobin A1c (HbA1c), reduced diabetes medications, and weight loss (mostly over shorter term) [31]. While some benefits may remain in pregnancy, the safety of a ketogenic diet in pregnancy has not been established.

Opposing Evidence

A study done in children with type 1 diabetes demonstrated ketone bodies rapidly accumulate in the brain during episodes of DKA. From this, it has been hypothesized ketone bodies may have a direct effect on the brain microvasculature and blood brain barrier permeability, yielding the brain more vulnerable to oxidative damage [42, 43]. Although ketones may be used as an alternative efficient energy substrate, high levels of ketones can inhibit de novo pyrimidine synthesis thereby slowing down the rate of cellular growth by impairing nucleotide biosynthesis (the building blocks for DNA and RNA) [43]. In juvenile rats, ketosis led to significant reductions in blood flow to the cerebral cortex and striatum compared to controls [44]. In fact, long-term ketonemia in rats has been noted to reduce glucose utilization to levels observed in metabolic encephalopathies [45].

In a sequence of more recent studies conducted by Sussman and her colleagues, murine embryos of a

gestational mother consuming a ketogenic diet exhibited embryonic growth retardation and alterations in brain anatomy in utero resulting in smaller pups and decreased litter size [43, 46]. The authors found a gestational ketogenic diet reduced maternal fertility and increased susceptibility to fatal maternal ketoacidosis during lactation [43]. In fact, investigators had to remove pups from the ketogenic diet litter to join the standard diet litter to ensure viability. However, despite the adopted pups receiving adequate postnatal nutrition, they continued to exhibit growth retardation and poor weight gain when compared to pups of the standard diet mother. The alterations in mouse brain anatomy persisted on postnatal neuroimaging [43]. Although the evidence from animal models is compelling, it should be interpreted with the limitations of interpreting the presence of ketones in pregnancy in mind.

An older, non-randomized study conducted in 1991 by Rizzo et al. of 223 pregnant women (n = 99 GDM, n = 89pre-existing diabetes, n = 35 no diabetes) found offspring intellectual developmental scores at 2 years of age correlated inversely with maternal third-trimester ketones, specifically β -hydroxybutyrate levels (p < 0.01). The same inverse correlation was found with offspring developmental scores ages 3 to 5 (p < 0.02). This association persisted despite attainment of adequate maternal glycemic control in second and third trimesters (HbA1c 5.3–6.2%). The authors noted the more aberrant the maternal metabolism was, the lower the offspring scores were, attesting to the sensitivity of developmental events to maternal ketones [47].

There is a lack of randomized trials examining short- and long-term consequences of gestational ketogenic diet in humans, with major concerns regarding the impact of prolonged maternal ketosis on fetal brain development. Additionally, extrapolating from concerns surrounding lowcarbohydrate diets, the potential unintended consequences of increased maternal fat intake are similarly applicable to the gestational ketogenic diet.

Low Glycemic Index Diet

Definition

The GI estimates the glucose response to intake of a carbohydrate food. The GI ranks food items on a scale of 0 to 100, with higher GI index values indicating a greater and more acute increase in blood glucose after ingestion. Food items with a GI of < 55 are considered low GI foods [48]. Diabetes Canada provides an excellent overview of further benefits and examples of low GI foods here: https://www. diabetes.ca/managing-my-diabetes/tools%2D%2D-resources/ the-glycemic-index-(gi).

Supporting Evidence

Low GI foods are effective in improving glucose levels in pregnant women with diabetes [49], as well as HbA1c in non-pregnant individuals with type 2 diabetes [50]. Likely a result of reduced postprandial hyperglycemia, low GI diets are associated with improved insulin sensitivity, reduced insulin requirements, and decreased need for diabetes medications inside and outside of pregnancy [31, 51, 52]. They are inherently less restrictive as low GI diets support a more liberalized intake of high-quality, complex carbohydrates with higher fiber content. In addition to GI, adjustments for dietary fiber may have additional benefits in GDM by indirectly lowering postprandial hyperglycemia by slowing food absorption and promoting gastrointestinal transport [53]. Despite these advantages, trials examining the effect of low GI diets on maternal and neonatal outcomes in GDM have conflicting results.

The first randomized controlled trial to examine the impact of a low GI diet for women (n = 63) with GDM was conducted by Moses et al. in 2009. The authors found the need to start insulin was reduced by 50% in the low GI group. Additionally, participants in the higher GI group could avoid insulin by switching to the low GI group. No differences were found in other reported pregnancy outcomes [54]. Another randomized controlled trial published in 2011 found no significant differences in pregnancy outcomes or need for insulin therapy between a low GI vs. conventional diet in GDM [55]. However, the mean GI achieved by women in both groups in this study was similar (low GI group = 46.8 ± 5.4 vs conventional = 52.4 ± 4.4), which may have contributed to these negative findings [55].

To clarify the association, Wei et al. conducted a systematic review and meta-analysis of five randomized controlled trials (n = 302) examining the effect of a low GI diet on maternal and neonatal outcomes in GDM. The authors reported a significantly lower risk of macrosomia (p = 0.008) and insulin usage (p = 0.01) in the low GI groups compared to control group. A subgroup analysis revealed a further reduction in risk of macrosomia in low GI diets with increased dietary fiber intake, relative to the control diet [56•]. The previously mentioned meta-analysis by Viana et al. included four trials (n =257) evaluating low GI diets. The GI scores in the low GI dietary intervention ranged from 47 to 49 (mean 48.9) compared to 47 to 58 (mean 53.5) in the control groups. Remarkably, a low GI diet was the only confirmed advantageous dietary intervention and was associated with less frequent maternal insulin use (p = 0.039) and lower newborn birth weight (p < 0.0001) [24].

Opposing Evidence

To our knowledge, there are no major safety concerns with a low GI diet as it inherently promotes well-balanced macronutrient intake with a focus on high-quality nutrition. However, food insecurity and access to high-quality foods may limit its applicability on a local and global scale. Although the low GI diet allows for a wide range of culturally adaptable foods, healthier diets are typically more costly and less available in low-income neighborhoods [57]. Additionally, food insecurity is an independent risk factor for suboptimal glycemic control [58].

Caloric Restriction

Definition

Severe caloric restriction is defined as total intake of < 1500 kcal/day or 50% reduction from pre-pregnancy caloric intake. Moderate caloric restriction is 1600–1800 kcal/day or 30% reduction from pre-pregnancy caloric intake [13].

Supporting Evidence

Evidence outside of pregnancy demonstrates caloric restriction leads to improved glycemic control and weight loss [31]. However, caloric restriction in pregnancy must be monitored closely as it can result in a predominantly fat-utilizing state with development of maternal ketosis [13, 59]. Additionally, it must be balanced with adequate gestational weight gain and fetal growth [60].

Two older randomized trials found a moderate caloric restriction in overweight/obese pregnant women with overt diabetes or GDM improved glycemic control without inducing maternal ketosis or compromising fetal growth [13, 16, 61]. Conversely, a severe caloric restriction improved glycemic control but led to ketonuria which was of unclear clinical significance as postnatal fetal outcomes were not assessed [16].

Opposing Evidence

Viana et al. reviewed two randomized controlled trials that compared moderate energy restriction to standard GDM nutrition (n = 425) and found no difference in cesarean-section rates, macrosomia, or neonatal hypoglycemia [24]. The Cochrane review by Han et al. similarly found no benefit of energy-restricted diets on perinatal outcomes [23]. Equally, both reviews did not find any adverse maternal or neonatal effects of energy restriction in GDM [23, 24]. While there were no significant improvements in maternal or neonatal outcomes found, these studies may have lacked adequate power to show a significant difference.

Mediterranean Diet

Definition

The Mediterranean diet is characterized by high consumption of vegetables, fruits, nuts, seeds, legumes, and unprocessed grains, as well as liberal use of olive oil. There is moderate intake of fish and poultry and limited consumption of dairy products, red meat, processed meats, or refined sugars. It typically has a lower GI and is rich in antioxidants and antiinflammatory foods [62, 63].

Supporting Evidence

A Mediterranean diet outside of pregnancy has shown to have beneficial effects on cardiovascular health, risk of diabetes, and obesity [62, 64, 65]. Currently, there is limited evidence in pregnancy as only one group has evaluated a Mediterranean diet in GDM.

The St Carlos GDM Prevention Study was a randomized controlled trial conducted in Spain that compared the impact of early adoption of a Mediterranean diet (8-12 weeks' gestation) to a conventional diet on the development of GDM in 874 pregnant women. Investigators found the Mediterranean diet reduced the incidence of GDM and decreased several perinatal outcomes including insulin-treated GDM, preterm delivery, emergency cesarean-sections, perineal trauma, and small for gestational age and LGA [66]. A post hoc analysis comparing women with GDM to normal glucose tolerance found treatment of GDM with a Mediterranean diet had no significant difference in excessive weight gain, pregnancyinduced hypertension, mode of delivery, perineal trauma, preterm delivery, and LGA between groups [63]. This suggests a Mediterranean diet was effective nutrition therapy in this group of women with GDM. However, since this was not a randomized control trial of women with GDM, we cannot assess its efficacy compared to standard dietary advice. Further studies are needed to establish efficacy and reproducibility of this diet outside of Spain-particularly in North America and Western Europe.

Limitations of the Evidence

Trials concerning nutrition therapy are notoriously challenging to conduct and compare because food intake is influenced by numerous social, financial, and psychological factors [22]. Food insecurity and access to high-quality foods influence patient adherence and overall glycemic control [57, 58]. Despite systematic reviews revealing no major differences between diets, the individual trials included were likely under-powered to find differences with very few reporting if they were adequately powered [17•]. Lastly, results of dietary intervention trials in this population must be interpreted cautiously as we cannot definitively conclude improvements in maternal glycemia and birth weight are secondary to reduced overall caloric intake, improved nutrient quality, or other modifications in macronutrient intake [17•].

Conclusions

Based on the available evidence, no particular diet can be recommended as the sole nutrition therapy in this heterogeneous, multi-cultural population of women with GDM. However, the low GI diet has *most* consistently demonstrated improved glycemic control, reduced maternal insulin use, and decreased neonatal birth weights in systematic reviews. The Mediterranean diet is promising as it is typically compromised of higher-quality, lower GI sources of food; however, its effectiveness in GDM is yet to be established. Currently, the ketogenic and calorie-restricted diets lack high-quality evidence and further studies are needed to determine their efficacy and safety in GDM. Table 2 summarizes the recommended GDM diets included in this review.

The low GI diet and high-complex carbohydrate intake frequently go together as they both represent nutrition plans that emphasize high-quality carbohydrates which tend to contain more vitamins and minerals, are higher in fiber, and calorically adequate [22, 48]. Liberalizing maternal intake of highquality, nutrient-dense carbohydrates has been shown to lower maternal FFA production, leading to improved insulin action and a reduction in excess fetal fat accretion [22, 37•, 39]. Finally, and perhaps most importantly, a less carbohydraterestrictive approach may be more acceptable to women with GDM as it is more culturally adaptable, reduces maternal anxiety surrounding food choices, and may improve long-term adherence [22, 28, 67]. The low GI, high-complex carbohydrate diet has the potential to promote a healthier and more sustainable diet extending into the postpartum period, which is paramount given the increased risk of developing type 2 diabetes in these women. The Diabetes Canada, National Institute for Health and Care Excellence (NICE), and the International Diabetes Federation (IDF) guidelines recommend replacing high GI foods with low GI foods in GDM nutrition therapy [19–21]. Emerging evidence supports a well-balanced diet, characterized by high-quality complex carbohydrates with low GI and high fiber content, is associated with improved perinatal outcomes in GDM with no evidence of harm. However, larger adequately powered studies are still needed to further clarify this association and to establish the most effective method of dietary counseling in this group of women.

Authors' Contributions AM and JY contributed the design and drafting of the paper. AM prepared the manuscript, which all authors critically reviewed. All the authors were fully responsible for all the content, and editorial decisions were involved at all stages of the manuscript development and have approved the final version.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:

- · Of importance
- Metzger BE, Gabbe SG, Persson B, Buchanan TA, Catalano PA, Damm P, et al. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care. 2010;33(3):676–82.
- Guariguata L, Linnenkamp U, Beagley J, Whiting DR, Cho NH. Global estimates of the prevalence of hyperglycaemia in pregnancy. Diabetes Res Clin Pract. 2014;103(2):176–85.
- Catalano PM, McIntyre HD, Cruickshank JK, McCance DR, Dyer AR, Metzger BE, et al. The hyperglycemia and adverse pregnancy outcome study: associations of GDM and obesity with pregnancy outcomes. Diabetes Care. 2012;35(4):780–6.
- American Diabetes A. 13. Management of diabetes in pregnancy: standards of medical care in diabetes-2018. Diabetes Care. 2018;41(Suppl 1):S137–S43.
- Simmons D. Diabetes and obesity in pregnancy. Best Pract Res Clin Obstet Gynaecol. 2011;25(1):25–36.
- Kim SY, England L, Wilson HG, Bish C, Satten GA, Dietz P. Percentage of gestational diabetes mellitus attributable to overweight and obesity. Am J Public Health. 2010;100(6):1047–52.
- Chen C, Xu X, Yan Y. Estimated global overweight and obesity burden in pregnant women based on panel data model. PLoS One. 2018;13(8):e0202183.
- Diagnostic criteria and classification of hyperglycaemia first detected in pregnancy: a World Health Organization Guideline. Diabetes Res Clin Pract. 2014;103(3):341–63.
- Group HSCR, Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, et al. Hyperglycemia and adverse pregnancy outcomes. N Engl J Med. 2008;358(19):1991–2002.
- Sermer M, Naylor CD, Gare DJ, Kenshole AB, Ritchie JW, Farine D, et al. Impact of increasing carbohydrate intolerance on maternalfetal outcomes in 3637 women without gestational diabetes. The Toronto tri-hospital gestational diabetes project. Am J Obstet Gynecol. 1995;173(1):146–56.
- Egan AM, Simmons D. Lessons learned from lifestyle prevention trials in gestational diabetes mellitus. Diabet Med. 2019;36(2):142– 50.
- Jiwani A, Marseille E, Lohse N, Damm P, Hod M, Kahn JG. Gestational diabetes mellitus: results from a survey of country prevalence and practices. J Matern Fetal Neonatal Med. 2012;25(6): 600–10.
- Blumer I, Hadar E, Hadden DR, Jovanovic L, Mestman JH, Murad MH, et al. Diabetes and pregnancy: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2013;98(11):4227–49.

- Hartling L, Dryden DM, Guthrie A, Muise M, Vandermeer B, Donovan L. Benefits and harms of treating gestational diabetes mellitus: a systematic review and meta-analysis for the U.S. preventive services task force and the National Institutes of Health Office of medical applications of research. Ann Intern Med. 2013;159(2):123–9.
- Landon MB, Spong CY, Thom E, Carpenter MW, Ramin SM, Casey B, et al. A multicenter, randomized trial of treatment for mild gestational diabetes. N Engl J Med. 2009;361(14):1339–48.
- Knopp RH, Magee MS, Raisys V, Benedetti T, Bonet B. Hypocaloric diets and ketogenesis in the management of obese gestational diabetic women. J Am Coll Nutr. 1991;10(6):649–67.
- 17.• Yamamoto JM, Kellett JE, Balsells M, Garcia-Patterson A, Hadar E, Sola I, et al. Gestational diabetes mellitus and diet: a systematic review and meta-analysis of randomized controlled trials examining the impact of modified dietary interventions on maternal glucose control and neonatal birth weight. Diabetes Care. 2018;41(7): 1346–61. Results of this systematic review and meta-analysis revealed modified dietary interventions, beyond the typical dietary advice for GDM, resulted in improved maternal glycemic control and infant birthweight outcomes.
- Garcia-Patterson A, Balsells M, Yamamoto JM, Kellett JE, Sola I, Gich I, et al. Usual dietary treatment of gestational diabetes mellitus assessed after control diet in randomized controlled trials: subanalysis of a systematic review and meta-analysis. Acta Diabetol. 2019;56(2):237–40.
- Diabetes Canada Clinical Practice Guidelines Expert C, Feig DS, Berger H, Donovan L, Godbout A, Kader T, et al. Diabetes and pregnancy. Can J Diabetes. 2018;42(Suppl 1):S255–S82.
- 20. National Collaborating Centre for Ws, Children's H. National Institute for Health and Care Excellence: clinical guidelines. Diabetes in pregnancy: management of diabetes and its complications from preconception to the postnatal period. London: National Institute for Health and Care Excellence (UK) Copyright (c) 2015 National Collaborating Centre for Women's and Children's Health.; 2015.
- IDF Clinical Guidelines Task Force. Global Guideline on Pregnancy and Diabetes. Brussels: International Diabetes Federation. 2009.
- 22. Hernandez TL, Mande A, Barbour LA. Nutrition therapy within and beyond gestational diabetes. Diabetes Res Clin Pract. 2018;145:39–50.
- Han S, Middleton P, Shepherd E, Van Ryswyk E, Crowther CA. Different types of dietary advice for women with gestational diabetes mellitus. Cochrane Database Syst Rev. 2017;2:Cd009275.
- Viana LV, Gross JL, Azevedo MJ. Dietary intervention in patients with gestational diabetes mellitus: a systematic review and metaanalysis of randomized clinical trials on maternal and newborn outcomes. Diabetes Care. 2014;37(12):3345–55.
- Hernandez TL. Carbohydrate content in the GDM diet: two views: view 1: nutrition therapy in gestational diabetes: the case for complex carbohydrates. Diabetes Spectr. 2016;29(2):82–8.
- Elidottir AS, Halldorsson TI, Gunnarsdottir I, Ramel A. Dietary intake and cardiovascular risk factors in Icelanders following voluntarily a low carbohydrate diet. PLoS One. 2016;11(8):e0156655.
- 27. Derbyshire E, Davies J, Costarelli V, Dettmar P. Diet, physical inactivity and the prevalence of constipation throughout and after pregnancy. Matern Child Nutr. 2006;2(3):127–34.
- Hui AL, Sevenhuysen G, Harvey D, Salamon E. Stress and anxiety in women with gestational diabetes during dietary management. Diabetes Educ. 2014;40(5):668–77.
- Hui AL, Sevenhuysen G, Harvey D, Salamon E. Food choice decision-making by women with gestational diabetes. Can J Diabetes. 2014;38(1):26–31.

- van Wyk HJ, Davis RE, Davies JS. A critical review of lowcarbohydrate diets in people with type 2 diabetes. Diabet Med. 2016;33(2):148–57.
- Feinman RD, Pogozelski WK, Astrup A, Bernstein RK, Fine EJ, Westman EC, et al. Dietary carbohydrate restriction as the first approach in diabetes management: critical review and evidence base. Nutrition. 2015;31(1):1–13.
- Jovanovic-Peterson L, Peterson CM. Dietary manipulation as a primary treatment strategy for pregnancies complicated by diabetes. J Am Coll Nutr. 1990;9(4):320–5.
- Peterson CM, Jovanovic-Peterson L. Percentage of carbohydrate and glycemic response to breakfast, lunch, and dinner in women with gestational diabetes. Diabetes. 1991;40(Suppl 2):172–4.
- Major CA, Henry MJ, De Veciana M, Morgan MA. The effects of carbohydrate restriction in patients with diet-controlled gestational diabetes. Obstet Gynecol. 1998;91(4):600–4.
- Cypryk K, Kaminska P, Kosinski M, Pertynska-Marczewska M, Lewinski A. A comparison of the effectiveness, tolerability and safety of high and low carbohydrate diets in women with gestational diabetes. Endokrynol Pol. 2007;58(4):314–9.
- Moreno-Castilla C, Hernandez M, Bergua M, Alvarez MC, Arce MA, Rodriguez K, et al. Low-carbohydrate diet for the treatment of gestational diabetes mellitus: a randomized controlled trial. Diabetes Care. 2013;36(8):2233–8.
- 37.• Hernandez TL, Van Pelt RE, Anderson MA, Reece MS, Reynolds RM, de la Houssaye BA, et al. Women with gestational diabetes mellitus randomized to a higher-complex carbohydrate/low-fat diet manifest lower adipose tissue insulin resistance, inflammation, glucose, and free fatty acids: a pilot study. Diabetes Care. 2016;39(1): 39–42. Results of this highly controlled pilot study resulted in improved maternal glycemic control and metabolic parameters with a high-complex carbohydrate/low fat diet when compared to low-carbohydrate diet.
- Butte NF. Carbohydrate and lipid metabolism in pregnancy: normal compared with gestational diabetes mellitus. Am J Clin Nutr. 2000;71(5 Suppl):1256S–61S.
- 39. Hernandez TL, Sutherland JP, Wolfe P, Allian-Sauer M, Capell WH, Talley ND, et al. Lack of suppression of circulating free fatty acids and hypercholesterolemia during weight loss on a high-fat, low-carbohydrate diet. Am J Clin Nutr. 2010;91(3):578–85.
- 40. Schaefer-Graf UM, Graf K, Kulbacka I, Kjos SL, Dudenhausen J, Vetter K, et al. Maternal lipids as strong determinants of fetal environment and growth in pregnancies with gestational diabetes mellitus. Diabetes Care. 2008;31(9):1858–63.
- Barry D, Ellul S, Watters L, Lee D, Haluska R Jr, White R. The ketogenic diet in disease and development. Int J Dev Neurosci. 2018;68:53–8.
- Dalfra MG, Burlina S, Sartore G, Lapolla A. Ketoacidosis in diabetic pregnancy. J Matern Fetal Neonatal Med. 2016;29(17):2889–95.
- 43. Sussman D, Ellegood J, Henkelman M. A gestational ketogenic diet alters maternal metabolic status as well as offspring physiological growth and brain structure in the neonatal mouse. BMC Pregnancy Childbirth. 2013;13:198.
- Glaser N, Ngo C, Anderson S, Yuen N, Trifu A, O'Donnell M. Effects of hyperglycemia and effects of ketosis on cerebral perfusion, cerebral water distribution, and cerebral metabolism. Diabetes. 2012;61(7):1831–7.
- al-Mudallal AS, Levin BE, Lust WD, Harik SI. Effects of unbalanced diets on cerebral glucose metabolism in the adult rat. Neurology. 1995;45(12):2261–5.
- 46. Sussman D, van Eede M, Wong MD, Adamson SL, Henkelman M. Effects of a ketogenic diet during pregnancy on embryonic growth in the mouse. BMC Pregnancy Childbirth. 2013;13:109.

- Rizzo T, Metzger BE, Burns WJ, Burns K. Correlations between antepartum maternal metabolism and intelligence of offspring. N Engl J Med. 1991;325(13):911–6.
- 48. Augustin LS, Kendall CW, Jenkins DJ, Willett WC, Astrup A, Barclay AW, et al. Glycemic index, glycemic load and glycemic response: an international scientific consensus summit from the international carbohydrate quality consortium (ICQC). Nutr Metab Cardiovasc Dis. 2015;25(9):795–815.
- Lock DR, Bar-Eyal A, Voet H, Madar Z. Glycemic indices of various foods given to pregnant diabetic subjects. Obstet Gynecol. 1988;71(2):180–3.
- Brand-Miller JC, Petocz P, Colagiuri S. Meta-analysis of lowglycemic index diets in the management of diabetes: response to Franz. Diabetes Care. 2003;26(12):3363–4 author reply 4-5.
- Moses RG, Luebcke M, Davis WS, Coleman KJ, Tapsell LC, Petocz P, et al. Effect of a low-glycemic-index diet during pregnancy on obstetric outcomes. Am J Clin Nutr. 2006;84(4):807–12.
- Barr S, Reeves S, Sharp K, Jeanes YM. An isocaloric low glycemic index diet improves insulin sensitivity in women with polycystic ovary syndrome. J Acad Nutr Diet. 2013;113(11):1523–31.
- Zhang C, Liu S, Solomon CG, Hu FB. Dietary fiber intake, dietary glycemic load, and the risk for gestational diabetes mellitus. Diabetes Care. 2006;29(10):2223–30.
- Moses RG, Barker M, Winter M, Petocz P, Brand-Miller JC. Can a low-glycemic index diet reduce the need for insulin in gestational diabetes mellitus? A randomized trial. Diabetes Care. 2009;32(6): 996–1000.
- 55. Louie JC, Markovic TP, Perera N, Foote D, Petocz P, Ross GP, et al. A randomized controlled trial investigating the effects of a lowglycemic index diet on pregnancy outcomes in gestational diabetes mellitus. Diabetes Care. 2011;34(11):2341–6.
- 56.• Wei Y, Jin Z, Shen G, Zhao X, Yang W, Zhong Y, et al. Effects of intensive antihypertensive treatment on Chinese hypertensive patients older than 70 years. J Clin Hypertens (Greenwich). 2013;15(6):420–7. Results of this systematic review and meta-analysis provide evidence that women with GDM following a low GI diet have lower rates of insulin use and decreased risk of neonatal macrosomia compared to control diets.
- Drewnowski A, Darmon N. Food choices and diet costs: an economic analysis. J Nutr. 2005;135(4):900–4.
- Seligman HK, Jacobs EA, Lopez A, Tschann J, Fernandez A. Food insecurity and glycemic control among low-income patients with type 2 diabetes. Diabetes Care. 2012;35(2):233–8.
- 59. Moreno-Castilla C, Mauricio D, Hernandez M. Role of medical nutrition therapy in the management of gestational diabetes mellitus. Curr Diab Rep. 2016;16(4):22.

- Catalano PM, Mele L, Landon MB, Ramin SM, Reddy UM, Casey B, et al. Inadequate weight gain in overweight and obese pregnant women: what is the effect on fetal growth? Am J Obstet Gynecol. 2014;211(2):137.e1–7.
- Rae A, Bond D, Evans S, North F, Roberman B, Walters B. A randomised controlled trial of dietary energy restriction in the management of obese women with gestational diabetes. Aust N Z J Obstet Gynaecol. 2000;40(4):416–22.
- 62. Estruch R, Ros E, Salas-Salvado J, Covas MI, Corella D, Aros F, et al. Primary prevention of cardiovascular disease with a Mediterranean diet supplemented with extra-virgin olive oil or nuts. N Engl J Med. 2018;378(25):e34.
- 63. Assaf-Balut C, Garcia de la Torre N, Duran A, Fuentes M, Bordiu E, Del Valle L, et al. Medical nutrition therapy for gestational diabetes mellitus based on Mediterranean diet principles: a subanalysis of the St Carlos GDM Prevention Study. BMJ Open Diabetes Res Care. 2018;6(1):e000550.
- 64. Estruch R, Martinez-Gonzalez MA, Corella D, Salas-Salvado J, Fito M, Chiva-Blanch G, et al. Effect of a high-fat Mediterranean diet on bodyweight and waist circumference: a prespecified secondary outcomes analysis of the PREDIMED randomised controlled trial. Lancet Diabetes Endocrinol. 2016;4(8):666–76.
- 65. Salas-Salvado J, Bullo M, Babio N, Martinez-Gonzalez MA, Ibarrola-Jurado N, Basora J, et al. Reduction in the incidence of type 2 diabetes with the Mediterranean diet: results of the PREDIMED-Reus nutrition intervention randomized trial. Diabetes Care. 2011;34(1):14–9.
- 66. Assaf-Balut C, Garcia de la Torre N, Duran A, Fuentes M, Bordiu E, Del Valle L, et al. A Mediterranean diet with additional extra virgin olive oil and pistachios reduces the incidence of gestational diabetes mellitus (GDM): a randomized controlled trial: the St. Carlos GDM prevention study. PLoS One. 2017;12(10):e0185873.
- 67. Teixeira PJ, Carraca EV, Marques MM, Rutter H, Oppert JM, De Bourdeaudhuij I, et al. Successful behavior change in obesity interventions in adults: a systematic review of self-regulation mediators. BMC Med. 2015;13:84.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.