ISSN 2959-409X

The Impact of Macronutrient and Dietary Patterns on Gestational Diabetes Mellitus

Nike Tan[1, *]

[1] University of Alberta, Edmonton, Canada
*Corresponding author: nike1@ualberta.ca

Abstract:

Pregnancy is a physiological condition that increases insulin resistance (IR) due to hormonal changes, including elevated levels of estrogen, progesterone, and human placental lactogen (HPL). Such IR, especially in the later stages of pregnancy, can cause gestational diabetes mellitus (GDM), characterized by glucose intolerance first detected during pregnancy. GDM poses significant health risks for both the mother and the fetus, including the potential for pre-eclampsia, emergency C-sections, and type 2 diabetes (T2D) for the mother, as well as preterm birth, hypoglycemia, and being large for gestational age (LGA) for the baby. Proper dietary modifications can help regulate blood sugar levels, improve insulin sensitivity, and ensure healthy gestational weight gain (GWG), thereby reducing the possibility of undesirable outcomes. This paper discusses the role of energy, carbohydrate, fat, and protein, and compares the effects of the Mediterranean diet (MD) and Western diet (WD) on the risk of GDM. The main objective of this paper is to identify the most effective dietary strategies for preventing and managing GDM. The finding indicates that a MD rich in nutrient-dense foods, complex carbohydrates/lower GI, unsaturated fatty acids (FAs), and balanced protein has beneficial effects on GDM. In contrast, the WD with empty calories, simple carbohydrates/higher glycemic index (GI), saturated FAs (SFA), and animal-based protein increases the risk of GDM. Future studies should continue to explore the long-term effects of dietary interventions, integrate other lifestyle factors, and consider genetic differences to provide comprehensive management strategies for GDM.

Keywords: Macronutrient; dietary patterns; gestational diabetes mellitus (GDM).

1. Introduction

Pregnancy is widely recognized as a physiological state that can lead to the development of IR. As pregnancy progresses, a rise in hormones such as estrogen, progesterone, leptin, cortisol, and HPL together induce the IR. Particularly during late pregnancy, the increased placental secretion of HPL reduces the sensitivity of maternal peripheral tissues to insulin. This physiological adaptation allows the maternal body to utilize non-glucose fuel sources and save glucose for fetal growth. However, in some pregnant women, significant IR can result in elevated blood glucose levels and the onset of GDM. GDM is defined as any degree of glucose intolerance first identified during pregnancy. High-risk groups include women aged over 35 years, those with obesity, uncontrolled weight gain, low educational attainment, a family history of T2D, and a history of delivering a macrocosmic infant. Unmanaged GDM can lead to various complications, including an increased risk of preeclampsia, cesarean birth, and the later development of T2D in the mother. For the infant, risks include preterm birth, neonatal hypoglycemia, and being LGA. In recent years, there has been a substantial increase in GDM cases, largely attributed to sedentary lifestyles, stress, and high-calorie diets in urban populations worldwide. A meta-analysis conducted in the United States and Canada, encompassing 36 independent studies with a combined total of 1,550,917 women, found an overall average prevalence of GDM of 6.9% [1].

Preventing the onset of GDM and developing effective management strategies are crucial for ensuring positive pregnancy outcomes. Data from research demonstrates that lifestyle changes alone can manage blood glucose levels in 70–85% of females with GDM [2]. One of the key strategies involves dietary modifications, particularly focusing on the balance and quality of macronutrients—carbohydrates, fats and proteins. Appropriate dietary patterns can help regulate blood glucose levels, enhance insulin sensitivity, and prevent excessive weight gain. Understanding the influence of macronutrients and overall dietary patterns on GDM is essential for creating targeted nutritional interventions that promote the health of both mothers and newborns. This research paper aims to investigate the impact of macronutrients and energy intake on GDM. By comparing various dietary patterns, the study seeks to identify the most suitable macronutrients and foods for preventing and managing GDM effectively, thereby supporting maternal and fetal health during pregnancy.

2. The Impact of Macronutrients on GDM

2.1 Energy

During pregnancy, maternal weight gain is a complex process that involves fetal growth and development as well as multiple physiological changes in the mother. The weight of the fetus, placenta, and amniotic fluid accounts for the majority of weight gain, and the remaining weight gain is related to blood volume, tissue fluid, breast tissue, uterine expansion, and energy reserves. Based on pre-pregnancy BMI, the Institute of Medicine (IOM) recommends that women of different weight categories should gain within a specific range during pregnancy. Pregnant women with a BMI < 18.5 are recommended to gain 12.5 to 18 kg, pregnant women with a BMI between 18.5 to 24.9 are recommended to gain 11.5 to 16 kg, and pregnant women with a BMI between 25.0 to 29.9 should gain 7 to 11.5 kg. For pregnant women with a BMI ≥ 30, a weight gain of 5 to 9 kg is recommended.

Managing energy intake during pregnancy is particularly important because excessive energy intake may lead to excessive weight gain and increase the risk of GDM. Visceral fat accumulation has significant metabolic activity and can secrete a variety of inflammatory factors such as TNF-α, IL-6, and MCP-1, which can induce IR. Rapid weight gain in the first three months of pregnancy may weaken the ability of pancreatic B cells to secrete enough insulin to cope with the IR. In addition, obesity may reduce the level of insulin-like growth factor binding proteins, thereby increasing the bioavailability of insulin-like growth factor 1, further promoting fetal nutrient absorption, leading to fetal overgrowth, and triggering GDM-related metabolic problems. According to Teulings et al., an increase in BMI by 1 to 2 units during pregnancy increases the risk of GDM by 51%; an increase in BMI by 2-3 units and more than 3 units increases the risk by 81% and 137%, respectively [3].

For pregnant women with GDM, it is also crucial to control postpartum weight to reduce the risk of adverse perinatal outcomes. Recent studies have shown that good control of GWG is associated with better blood sugar management and pregnancy outcomes [4]. In particular, when the weight gain of GDM patients was lower than the IOM recommendation, the incidence of LGA was significantly reduced (OR=0.68, 95% CI 0.48-0.97), indicating a certain protective effect [4]. In contrast, weight gain exceeding the IOM recommendation increased the risk of LGA (OR=1.62, 95% CI 1.15-2.27) [4]. In addition, for every 2 kg of weight gain during pregnancy, the likelihood of using insulin treatment in GDM patients increased by 1.3 times, and the risk of giving birth to an LGA baby also increased by 1.4 times [5]. Therefore, appropriate energy intake during pregnancy is important to prevent excessive GWG and reduce GDM-related risks. In addition, GDM patients need to undergo strict weight management after delivery to reduce adverse perinatal outcomes like LGA.

Dietary carbohydrates play an essential role in maintaining glucose and lipid metabolism balance in pregnant mothers, as well as supporting the growth and development of the fetus. The IOM recommends that 45%-65% of energy intake come from carbohydrates, and all pregnant women should consume at least 175 grams of carbohydrates per day, including 28 grams of fiber. For pregnant mothers with GDM, adhering to a low-carbohydrate diet (about 40%) can positively impact metabolic outcomes, delivery methods, and the weight and health of the fetus [6]. However, some experts recommend focusing on the quality rather than the quantity of carbohydrates. Dietary carbohydrates are diverse, including simple sugars as well as longer-chain oligosaccharides and polysaccharides, each having different effects on blood glucose levels. Simple carbohydrates found in sweetened beverages, baked goods, candies, and processed foods lead to quick spikes in blood glucose. In contrast, complex carbohydrates, such as those found in whole grains, legumes, nuts, and vegetables, provide a slow release of glucose into the bloodstream and are preferable for managing blood glucose levels. Dietary fiber and resistant starch have structures that make them resistant to digestion or even completely non-digestible, which results in a slower rise in blood glucose. One study compared a low-carbohydrate, high-fat diet with a higher complex carbohydrate, lower-fat diet (CHOICE) in women with GDM. The CHOICE diet, which included 60% carbohydrates from complex sources and 25% fat, resulted in improved insulin sensitivity, lower fasting glucose levels, and reduced inflammation in adipose tissue [7]. Additionally, infants born to mothers on the CHOICE diet had lower adiposity, indicating potential long-term health benefits [7].

Building on this, the GI is a key indicator of the postprandial blood glucose response, showing how quickly consumed foods affect blood glucose levels after a meal. Carbohydrates that are rapidly absorbed and have a GI greater than 70 are classified as high GI foods, while those that are slowly absorbed and have a GI less than 55 are classified as low GI foods. One study in systematic reviews indicated that a low GI diet consistently shows improved glycemic control, reduced need for maternal insulin, and lower neonatal birth weights [8]. Additionally, research has also examined the impact of glycemic load (GL). The concept of GL combines both the quality (GI) and quantity (amount of carbohydrate) of carbohydrates in a food item. One study indicated that women in the highest tertile of GI or GL before pregnancy, in the first trimester, or during the second trimester had an increased risk of developing GDM by 12% (15%), 25% (23%), and 29% (25%) respectively, compared to those in the lowest tertile [9]. Another study suggested that the risk of GDM increased by 0.63% for each unit rise in GL [10]. Choosing low GI or low GL diets not only helps control the risk of GDM but may also have a positive impact on the long-term health of the mother and fetus. To sum up, either limiting carbohydrate consumption or replacing high-GI (GL) foods with slower-digesting alternatives can be effective strategies for managing GDM.

2.2 Fat

The IOM recommends that 20-35% of pregnant women's daily energy intake should come from fat and recommends limiting the intake of SFA found in whole-fat dairy products, meat with skin, lard, coconut oil, and palm oil. One study found that SFA intake of more than 10% of daily fat intake before and after pregnancy increased the risk of GDM [11]. SFA, especially palmitic acid (C16:0), accumulates in muscle and liver cells, leading to an increase in lipid intermediates such as diacylglycerol and ceramide, thereby weakening the cell's ability to respond to insulin and affecting glucose absorption. In addition, SFA is also associated with increased inflammatory responses because they can promote the production of proinflammatory cytokines by activating Toll-like receptors on immune cells, which may contribute to the occurrence of GDM.

Monounsaturated FAs (MUFA) are unsaturated FAs containing a single double bond, mainly found in foods such as olive oil and avocados. Studies have shown that MUFA can promote the secretion of GLP-1, thereby alleviating inflammation and improving glucose tolerance to a certain extent. Cohort studies have shown that women with higher MUFA levels in plasma phospholipids during gestational weeks 15 to 26 have a significantly reduced risk of GDM. Specifically, for every standard deviation increase in total MUFA levels of 18:1, the risk of GDM is reduced by 40% [12].

At the same time, polyunsaturated FAs (PUFA), especially n-3 PUFA, also help reduce the risk of GDM due to their anti-inflammatory properties. Studies have shown that pregnant women with the highest third of dietary n-3 FA intake have a 0.21-fold lower risk of GDM, while pregnant women with the highest intake of α-linolenic acid have a 0.15-fold lower risk of GDM [13]. n-3 and n-6 FAs are essential FAs that must be obtained through diet. They play a key role in cell membrane structure and the production of eicosanoids, which are particularly important for the development of the fetal nervous, immune, vascular, and visual systems. However, the balance between n-3 and n-6 PUFAs is critical. Modern diets are usually high in n-6 FAs, which may induce inflammation and offset the protective effects of n-3 FAs. Studies have shown that the dietary n-6 FA ratio of GDM patients is as high as 8.35, while that of the control group is 5.63 [14].

According to available evidence, raising MUFA and PUFA, particularly n-3 PUFA, can benefit moms' and babies' long-term health in addition to lowering the risk of GDM. There is a theoretical basis for improving the nutritional structure during pregnancy by limiting the intake of SFA, which successfully prevents fat accumulation and the inflammatory response linked to metabolic diseases. Additionally, even though most modern diets contain a significant amount of omega-6 FAs, maintaining the balance of inflammation and improving insulin sensitivity depend on a sensible adjustment of the omega-3 to omega-6 PUFA ratio.

2.3 Protein

Dietary protein may influence the development of GDM by causing pancreatic islets to become fatigued and fail. Every 5% increase in energy intake from total protein during pregnancy was related to a 20% increase in the risk of GDM [15]. This happens because the glucose threshold of the pancreatic islets decreases, prompting these cells to secrete more insulin. Increasing insulin secretion leads to enhanced gluconeogenesis and raises plasma glucagon levels. The recommended protein intake during pregnancy is 10–35% of the total daily energy intake. The recommended dietary allowance for pregnant women is 1.1 grams per kilogram of body weight per day or 71 grams of protein per day.

Animal proteins are complete proteins, as they contain all nine essential amino acids (AAs) that the body couldn't synthesize, while plant proteins, except for soybeans which are considered a complete source of protein for adults, are generally considered incomplete. However, a variety of plant-based proteins consumed throughout the day compensate for other's lack of AAs. While both animal and plant proteins contribute to the overall protein intake, animal proteins are more strongly associated with an increased risk of GDM. According to a dose-response study, consuming 4% to 10% of energy from animal proteins during pregnancy is linked to an elevated risk of

GDM [15]. However, the risk of GDM was not significantly correlated with the consumption of plant proteins [15]. The difference between animal-based AAs and planted-based AAs may be because branched-chain AAs (leucine, isoleucine, and valine), are more in animal proteins. Branched-chain AAs (BCAAs) found in high-quality proteins have been shown to activate the mechanistic target of the rapamycin pathway, which regulates insulin signaling and glucose uptake in cells. However, excessive intake of BCAAs can lead to inhibition of the insulin receptor substrate and further IR. Moreover, the catabolism of BCAAs produces metabolites that activate the NF-κB pathway, which is related to the activation promotes inflammation, and impairs insulin sensitivity. Therefore, managing the intake of animal-based proteins while limiting high overall protein intake may be beneficial in reducing the risk of GDM during pregnancy.

3. Dietary Patterns and GDM

While individual macronutrients like carbohydrates, fats, and protein play distinct roles in the development and management of GDM, it is essential to recognize that dietary patterns also influence this condition. Understanding how specific foods and combinations of nutrients interact can provide a more comprehensive picture of dietary influences on GDM. Therefore, this section will analyze the effect mechanisms of two different dietary patterns on the control and prevention of GDM.

3.1 Mediterranean Diet (MD)

The MD is a dietary pattern celebrated for its myriad health benefits. Originating from the traditional eating habits of countries bordering the Mediterranean Sea, such as Greece, Italy, and Spain, this diet fosters a balanced and sustainable way of eating. Adherence to the MD effectively manages GDM and reduces adverse pregnancy outcomes. Firstly, adherence to the MD promotes healthier weight gain during pregnancy by increasing satiety and slowing food digestion, which is crucial as excessive GWG is a known risk factor for GDM. Furthermore, the MD emphasizes low-GI foods. Fresh, wholesome, seasonal fruits and vegetables, tomatoes, cucumbers, peppers, and leafy greens are commonly featured in meals. Whole grains such as whole wheat bread, pasta, brown rice, bulgur, and barley are preferred over refined grains. Vegetables, fruits, and whole grains are rich in fiber and help maintain stable blood sugar levels, reducing the risk of spikes that are harmful for individuals with GDM. These foods can help manage intestinal inflammation by modifying gut microbiota and reducing the body's overall inflammatory response. The anti-inflammatory of the healthy FAs in MD can also mitigate the chronic inflammation and oxidative stress associated with GDM. Olive oil, rich in MUFA, is the primary fat source in the MD. Dairy products are consumed in moderation, typically in the form of cheese and yogurt, and eggs are recommended at zero to four servings a week, preventing the high SFA intake. n-3 FA-enriched fish and seafood are the primary sources of animal protein, consumed at least twice a week, while red meat and processed meat consumption is limited. A multivariable analysis showed that individuals in the highest tertile of the MD adherence score had a 41% lower risk of developing GDM compared to those in the lowest tertile [16]. A sub-analysis conducted by Duran et al. indicated that women following an MD had similar hemoglobin A1c levels, fasting insulin, and homeostasis model assessment of IR to those with normal glucose tolerance at 36-38 gestational weeks [17]. This diet helped maintain near-normoglycemia and reduced adverse pregnancy outcomes such as macrosomia and pregnancy-induced hypertensive disorders [17].

3.2 Western Diet (WD)

21 prospective cohort studies have shown that the WD pattern is highly correlated with the occurrence of GDM, with a risk ratio of 1.52 [18]. WD usually includes a large amount of high-sugar foods, sugary drinks, refined grains, red meat, and other high-calorie foods. This type of eating pattern interferes with the body's regulation of hunger and satiety, leading to an increase in BMI and IR, thereby increasing the risk of GDM. Among them, from a nutritional point of view, sweets and sugary drinks contain monosaccharides. Refined grains contain starch components that can be quickly digested, which can easily cause blood sugar to rise rapidly and weaken insulin sensitivity. Red meat contains a large amount of SFA and branched-chain amino acids (BCAA), both of which are closely related to the occurrence of insulin resistance and GDM. In particular, the heme iron in red meat may damage the function of pancreatic β cells by inducing reactive oxygen species (ROS), thereby reducing insulin secretion. In addition, WD contains red meat, which usually contains nitrites and nitrates during its processing. They may react with amino compounds in the body to form nitrosamines, which increase ROS and inflammatory responses, thereby affecting the expression of insulin receptors and further exacerbating insulin resistance. Finally, fried foods in WD, such as French fries, will produce Maillard reactions and form advanced glycation end products (AGEs) due to high cooking temperatures. After AGEs bind to their receptors, they will activate a series of signaling pathways, enhance inflammatory responses in pregnancy tissues, and may eventually lead to the development of GDM. Therefore, WD currently has relevant risk factors in the pathogene-

sis of GDM, both from the perspective of macronutrients and from the perspective of food processing. In the health management of pregnant women, the connection between balancing deliciousness and health needs should also be considered.

4. Conclusion

In conclusion, this paper focuses on the impact of macronutrients and dietary patterns on the risk and management of GDM. Keeping gestation weight gain within the recommended range of IOM guidelines is beneficial to the health of both mother and fetus. Carbohydrate management is essential to maintain blood sugar levels, this implies the consumption of complex carbohydrates and fiber rather than simple sugars. Similarly, the type of dietary fat also plays an important role, as unsaturated fats help to reduce inflammation and improve insulin sensitivity. Protein intake should be carefully managed to avoid excessive consumption of animal protein. The MD is rich in vegetables, whole grains, lean protein, and healthy fats, and it has shown promising results in promoting healthier weight gain, reducing inflammation, and controlling GDM. On the other hand, the WD, characterized by a high intake of sweets, refined grains, red meats, and processed foods, is strongly associated with an increased risk of GDM due to its contribution to obesity and IR. Monitoring weight gain, blood sugar, and fetal growth is important for adjusting nutritional recommendations that benefit both pregnant women and their babies.

However, this article does not address the role of micronutrients in managing GDM, the influence of genetic factors, and the long-term effects of dietary interventions on both mother and child post-pregnancy. Analyzing the roles of specific micronutrients and their interactions with macronutrients can provide a better understanding of optimal nutritional strategies for preventing and managing GDM. Moreover, the impact of physical activity and other lifestyle interventions on the risk and management of GDM remains unexplored. Future studies should follow long-term randomized controlled trials of mothers and their children after pregnancy.

References

[1] Eades CE, Burrows KA, Andreeva R, et al. Prevalence of gestational diabetes in the United States and Canada: a systematic review and meta-analysis. BMC Pregnancy and Childbirth, 2024, 24(1).

[2] American Diabetes Association. 13. Management of Diabetes in Pregnancy. Diabetes Care, 2017, 40: S114–S119.

[3] Teulings NEWD, Masconi KL, Ozanne SE, et al. Effect of interpregnancy weight change on perinatal outcomes: systematic review and meta-analysis. BMC Pregnancy and Childbirth, 2019, 19(1).

[4] He J, Hu K, Wang B, Wang H. Effects of women with gestational diabetes mellitus related weight gain on pregnancy outcomes and its experiences in weight management programs: a mixed-methods systematic review. Frontiers in Endocrinology, 2023, 14.

[5] Barnes RA, Wong T, Ross GP, et al. Excessive weight gain before and during gestational diabetes mellitus management: What is the impact?. Diabetes Care, 2019, 43(1): 74-81.

[6] Pasand M, Eslamian G, Noura P, et al. The effects of low carbohydrate diet on the outcomes of gestational diabetes: A systematic review. ijogi.mums.ac.ir, Published online June 22, 2023.

[7] Hernandez TL, Van Pelt RE, Anderson MA, 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, 2015, 39(1): 39-42.

[8] Mahajan A, Donovan LE, Vallee R, Yamamoto JM. Evidenced-Based Nutrition for gestational diabetes mellitus. Current Diabetes Report, 2019, 19(10).

[9] Zhang X, Gong Y, Della Corte K, et al. Relevance of dietary glycemic index, glycemic load and fiber intake before and during pregnancy for the risk of gestational diabetes mellitus and maternal glucose homeostasis. Clinical Nutrition, 2021, 40(5): 2791-2799.

[10] Zhang Y, Feng H, Li X, et al. Association of dietary glycemic index and glycemic load with the risk of gestational diabetes mellitus: a systematic review and dose-response meta-analysis. Gynecological Endocrinology, 2024, 40(1).

[11] Alamolhoda SH, Zare E, Mirabi P. Diet and Gestational Diabetes Mellitus: A Systematic Review study. Current Women's Health Reviews, 2023, 19(1).

[12] Tsoi KY, Zhu Y, Wu J, et al. Plasma phospholipid Monounsaturated Fatty Acids and Gestational Diabetes Mellitus: A Longitudinal study in the NICHD Fetal Growth Studies–Singletons Cohort. Diabetes, 2022, 71(12): 2707-2715.

[13] Barbieiri P, Nunes JC, Torres AG, et al. Indices of dietary fat quality during midpregnancy is associated with gestational diabetes. Nutrition, 2016, 32(6): 656-661.

[14] Fu Y, Yang Y, Zhu L, Chen J, Yu N, Zhao M. Effect of dietary n-6: n-3 Poly-Unsaturated fatty acids ratio on gestational diabetes mellitus: a prospective cohort. Gynecological Endocrinology, 2022, 38(7): 583-587.

[15] Hajhashemy Z, Bagherniya M, Sadeghi O, Askari G. The relation of dietary protein intake before and during the pregnancy with gestational diabetes mellitus (GDM): A GRADE-assessed systematic review and dose–response meta-analysis of epidemiologic studies. Clinical Nutrition, 2024, 43(2): 505-518.

[16] Mohtashaminia F, Hosseini F, Jayedi A, et al. Adherence to the Mediterranean diet and risk of gestational diabetes: a

prospective cohort study. BMC Pregnancy and Childbirth, 2023, 23(1).
[17] Duran A, Assaf-Balut C, De La Torre NG, et al. Medical Nutrition therapy for gestational diabetes mellitus (GDM) based on Mediterranean diet principles. Diabetes, 2018, 67(Supplement_1).
[18] Quan W, Zeng M, Jiao Y, et al. Western Dietary Patterns, Foods, and Risk of Gestational Diabetes Mellitus: A Systematic Review and Meta-Analysis of Prospective Cohort Studies. Advances in Nutrition, 2021, 12(4): 1353-1364.