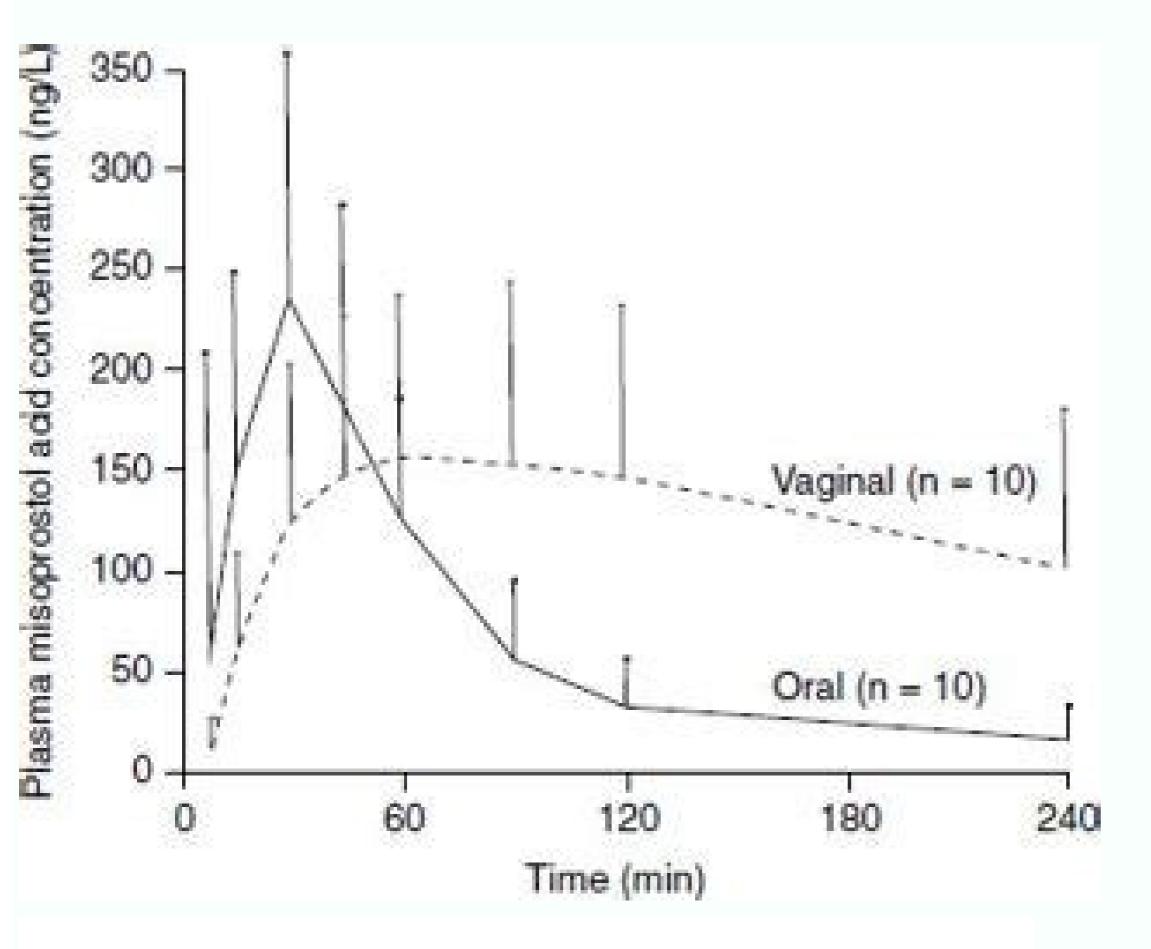




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# Clinical Management Guidelines for Obstetrician-Gynecologists

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Committee on Practice Bulletins—Obstetrics. This Practice Bulletin was developed by the American College of Obstetricians and Gynecologists. Committee on Practice Bulletins—Obstetrics with the assistance of Aaron B. Canghey, MD, PhD, and Mark Turnentine, MD.

INTERIM UPDATE: This Practice Bulletin is updated as highlighted to reflect a limited, focused change to clarify and provide additional information on the pharmacologic treatment of gestational diabetes mellitus.

# **Gestational Diabetes Mellitus**

Gestational diabetes mellitus (GDM) is one of the most common medical complications of pregnancy. However, debate continues to surround the diagnosis and treatment of GDM despite several recent large-scale studies addressing these issues. The purposes of this document are the following: 1) provide a brief overview of the understanding of GDM, 2) review management guidelines that have been validated by appropriately conducted clinical research, and 3) identify gaps in current knowledge toward which future research can be directed.

## Background

## **Definition and Prevalence**

Gestational diabetes mellitus is a condition in which carbohydrate intolerance develops during pregnancy. Gestational diabetes that is adequately controlled without medication is often termed diet-controlled GDM or class AIGDM. Gestational diabetes mellitus that requires medication to achieve euglycemia is often termed class. A2GDM. Because many women do not receive screening for diabetes mellitus before pregnancy, it can be challenging to distinguish GDM from preexisting diabetes. However, it has been estimated that in 2009, 7% of pregnancies were complicated by any type of diabetes and that approximately 86% of these cases represented women with GDM (1). Additionally, the prevalence of GDM varies in direct proportion to the prevalence of type 2 diabetes in a given population or racial or ethnic group. Caucasian women generally have the lowest rates of GDM. There is an increased prevalence of GDM among Hispanic, African American, Native American, and Asian or Pacific Islander women (2). Gestational diabetes also increases with the same risk factors seen for type 2 diabetes such as obesity and increased age (3). With a greater prevalence of obesity and sedentary lifestyles, the prevalence of GDM among reproductive-aged women is increasing globally.

### Maternal and Fetal Complications

Women with GDM have a higher risk of developing preeclampsia (9.8% in those with a fasting glucose less than 115 mg/dL and 18% in those with a fasting glucose greater than or equal to 115 mg/dL) and undergoing a cesarean delivery (25% of women with GDM who require medication and 17% of women with diet-controlled GDM underwent cesarean delivery versus 9.5% of controls) (4, 5). Furthermore, women with GDM have an increased risk of developing diabetes (predominantly type 2 diabetes) later in life. It is estimated that up to 70% of women with GDM will develop diabetes within 22-28 years after pregnancy (6-8). The progression to diabetes also is influenced by race, ethnicity, and obesity. For example, 60% of Latin American women with GDM may develop type 2 diabetes within 5 years of their index pregnancy (9).

The offspring of women with GDM are at increased risk of macrosomia, neonatal hypoglycemia, hyperbilirubinemia, shoulder dystocia, and birth trauma. There also is an increased risk of stillbirth, although how much this

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2017 Jul;296(1):35-41. 2016;95(22):e3792. 2019;19(10):94. Carbohydrate content in the GDM diet: two views: view 1: nutrition therapy in gestational diabetes: the case for complex carbohydrates. Agha-Jaffar R, Oliver N, Johnston D, Robinson S. 2014;99(6):1378-84. Several different types of dietary approaches are used globally, and there is no consensus among the various professional groups as to what constitutes an ideal approach. 2015;292(4):749-756. 2019;11(5):1003. doi:10.1016/j.fertnstert.2006.02.098Panchaud A, Rousson V, Vial T, et al. Nutrition therapy recommendations for the management of adults with diabetes. These included studies comparing a low-to-moderate GI diet versus a moderate high-GI diet; an energy-restricted diet versus a control diet; a low-carbohydrate diet; a low-carbohydr versus diet recommendations only; a soy protein-enriched diet versus no soy protein; a high-fibre diet versus a standard-fibre diet, characterized by intake of high-quality, complex carbohydrates, demonstrated lower insulin use and reduced risk of macrosomia. Pre-pregnancy adherence to the Mediterranean diet and gestational diabetes mellitus: a case-control study. 2010;2(2):339-51. Combined diet and exercise interventions for preventing gestational diabetes mellitus. Can a simple dietary screening in early pregnancy identify dietary habits associated with gestational diabetes? In a study by Vestgaard et al. 2019;9(7):e026908. Consuming 15 g to 20 g of glucose from a carbohydrate source should elevate glucose levels within 20 minutes and consider eating a snack with 15 g to 20 g of complex carbohydrates if their next meal is more than 30 minutes away to prevent recurring hypoglycemia. Conclusion Diagnosing GD early and managing it well decreases newborn complications and the risk of maternal preeclampsia. Jeanette Y. 2018;118(9):1719-42. People with diabetes on high-GI diets (>70) exhibit higher post-prandial values, and in non-pregnant patients with diabetes, low-GI diets lead to an additional 0.4% reduction in haemoglobin A1C [27]. Besides the conventional advice of restricting carbohydrates, studies demonstrate an important role for low-GI diets in GDM [13]. Medical nutrition therapy and lifestyle interventions. Supplement interventions with probiotics and myoinositol during pregnancy showed a decrease in the rates of GDM compared with a placebo [47, 50]. doi:10.1097/AOG.00000000001383Download Issue: May 2021 Association of Prenatal Care Expansion With Use of Antidiabetic Agents During Pregnancies Among Latina Emergency Medicaid Recipients With Gestational Diabetes. No part of this publication may be translated into other languages, reproduced or utilized in any form or by any means, electronic or mechanical, including photocopying, recording, microcopying, or by any information storage and retrieval system, without permission in writing from the publisher. Early diagnosis of GDM and earlier MNT intervention seem beneficial. An early pregnancy HbA1c ≥ 5.9% (41 mmol/mol) is optimal for detecting diabetes and identifies women at increased risk of adverse pregnancy outcomes. Obstet Gynecol. Mediterranean diet intervention advised early in the pregnancy or to pre-pregnant women has been shown to reduce GDM incidence and maternal-foetal adverse outcomes [44, 45]. Non-Nutritive SweetenersSeveral non-nutritive sweeteners have become available and are widely used by women, but their use during pregnancy, with only a couple of international guidelines approving the use of some of them during pregnancy. Cypryk K, Kamińska P, Kosiński M, Pertyńska-Marczewska M, Lewiński A. It is similar to the traffic light diet promoted in Australia [57] for healthy eating. Mapping foods according to red, yellow, and green colour codes helps in educating people on healthy foods and how processing and different cooking methods impact foods making healthy. Diabetes Care. Study results show a risk of fetal macrosomia 5 times higher in women with FBG levels of 100 to 105 mg/dL than in women with levels of 75 mg/dL.4Glycated hemoglobin A1c (HbA1c) goals tend to be lower in pregnant women.5 HbA1c levels at or exceeding 5.9% may predict adverse pregnancy outcomes.5 If hypoglycemia becomes a problem, raising the HbA1c goal to 7% is reasonable.3Medical TherapyAbout 20% of women with GD require insulin or oral antihyperglycemic agents. 2017;17(1):30. J Am Diet Assoc. 2014;37(5):1254-62. Effect of a high monounsaturated fatty acid diet on blood pressure and glucose metabolism in women with gestational diabetes mellitus. Prenatal Nutrition Guidelines for Health Professionals. Results showed that the intervention group had reduced incidence of GDM and improved several maternal and neonatal outcomes [43]. Artal R, Catanzaro RB, Gavard JA, Mostello DJ, Friganza JC. Int J Gynaecol Obstet. There is also greater motivation, sense of self-efficacy, and willingness to acquire new skills. Comparative effectiveness of metformin versus insulin for gestational diabetes in New Zealand. A pre-pregnancy low-carbohydrate diet with high protein and fat from vegetable food sources is not associated with the risk. I Matern Fetal Neonatal Med. 2014;37(11):2953-2959. Health Canada [12] in their pre-natal guidelines for health professionals has developed a GWG graph using the IOM guidelines for health professionals has developed a GWG graph using the IOM guidelines to monitor and motivate women to stay within the optimal weight gain range. There is limited research on caloric requirements and optimum weight gain for women with GDM, and a systemic review of the guidelines from various professional organizations shows varied recommendations. Moreno-Castilla C, Mauricio D, Hernandez M. It has been used as an educational tool which can be easily adapted to different regional and local foods across the world [56]. Nolan CJ. 2018;120(4):435-44. Association of whole grains, dairy and dietary fibre with neonatal outcomes in women with gestational diabetes mellitus: the WINGS project (WINGS-12). Birth weight above 4 kg was seen in 18% of MNT-treated GDM women versus 27 and 24% (p = 0.012) in non-diabetic and no MNT GDM women, respectively. 2007;30(Suppl 2):S188-93. Apart from the use of low-GI and high-fibre diets, another commonly used method to reduce high post-prandial levels and wide post-meal glucose, recommended by most guidelines, is distributing the total daily allocated carbohydrate portions into 3 small meals and 2-3 snacks per day [11]. FatMNT in GDM has primarily focussed on control of maternal glycaemia; however, data suggest that maternal lipids, especially triglycerides, may be stronger drivers of foetal growth than glucose [39, 40]. Increased consumption of total and saturated fat could worsen IR (Barbour LA, 2007) and increase foetal nutrient exposure, promoting overgrowth patterns. Academy of nutrition and dietetics gestational diabetes evidence-based nutrition practice guideline. Various simple tools to achieve these objectives are available, and in the absence of qualified dieticians, they can be used to train other health care professionals to provide nutrition counselling to women with GDM. Cochrane Database Syst Rev. While restricting carbohydrates helps control hyperglycaemia, substituting fat for carbohydrate, especially in obese women with pre-pregnancy insulin resistance (IR), could increase lipolysis and circulating free fatty acids (FFA) available for transplacental transfer leading to excess foetal fat accumulation, as well as worsening maternal IR [1, 21] which in turn may worsen hyperglycaemia in the mother [22]. To understand the effect of low carbohydrate on maternal IR, adipose tissue lipolysis, and infant adiposity, a randomized pilot study was undertaken by Hernandez et al. St. Leonards, NSW: Diabetes Education Centre, RNSH; 2010. Dietary intervention can reduce the risk of developing GDM and the proportion of infants born with macrosomia among pregnant women with obesity; physical activity interventions have not had the same effect. 2005;50(2). Diabetes and pregnancy: an Endocrine Society clinical practice guideline. Given the impact of GDM on the future health of the mother and offspring, these changes are not only relevant for the immediate pregnancy outcomes, but continued adherence, and Ponderal index compared with those born to mothers on the DASH diet had significantly lower weight, head circumference, and Ponderal index compared with those born to mothers on the control diet. 2019;11(7):1549. Kapur K, Kapur K, Kapur A. Effects of the biguanide class of oral hypoglycemic agents on mouse embryogenesis. All GDM participants were advised Mediterranean diets plus a recommended daily extra virgin olive oil intake ≥40 mL and a daily handful of nuts. Nutrients. The ACOG and ADA prefer insulin, because it does not cross the placenta.1 The FDA has not approved oral antihyperglycemic agents for GD. The IOM guideline does not provide any specific recommendation for women with GDM. 2015;25(9):795-815. Maternal lipids as strong determinants of fetal environment and growth in pregnancies with gestational diabetes: a metaanalysis. Medical nutrition therapy (MNT) is the bedrock for the management of gestational diabetes mellitus (GDM). Given the impact of GDM on the future health of the mother and offspring, dietary and lifestyle behaviour changes during pregnancy in women with GDM are not only relevant for immediate pregnancy outcomes, but continued adherence is also important for future health. doi:10.1111/bcp.13481Rowan JA, Rush EC, Plank LD, et al. 2017;1:CD006674. The average daily amount of fibre intake in each diet group was not stated. Filardi T, Panimolle F, Crescioli C, Lenzi A, Morano S. Evidenced-based nutrition for gestational diabetes mellitus. 2006;86(3):658-663. Randomized trial of metformin vs insulin in the management of gestational diabetes. Primary prevention of gestational diabetes mellitus through nutritional factors: a systematic review. The Indian guidelines recommend a minimum additional 23 g of protein intake daily during pregnancy over and above the normal recommended daily allowance for adult women. Protein intake restrictions may be required in presence of renal failure. Several specialized dietary protocols have also been tested in women are also more likely to exceed weight gain recommended for women. Overweight or obese pregnant women are also more likely to exceed weight gain recommended for women. Aspartame, saccharin, acesulfame, and sucralose are recommended by a few guidelines in moderate amounts. Excessive GWG, irrespective of pre-pregnancy and higher post-partum fat retention [7] which adds to the already high risk of future type 2 diabetes and cardiovascular disease in these women. 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. 2007;58(4):314-9. Meeting these targets is crucial. Endokrynol Pol. Visuals of portion sizes and use of household containers (cups and glass) as measures of food quantity are practical and easy teaching tools to help improve adherence to quantity of food consumed. Metformin in gestational diabetes: the offspring follow-up (MiG TOFU): body composition and metabolic outcomes at 7-9 years of age. Asemi Z, Tabassi Z, Samimi M, Fahiminejad T, Esmaillzadeh A. Luoto R, Laitinen K, Nermes M, Isolauri E. Hrolfsdottir I, Birgisdottir I, Birgisdottir I, Birgisdottir I, Birgisdottir I, Birgisdottir I, Smarason AK, Hardardottir H, et al. They also lower the risk of delayed postprandial hypoglycemia compared with human regular insulin.6 Insulin isophane suspension (NPH) is the intermediate/long-acting insulin detemir, and glargine have not been associated with pregnancy-related complications. [54] recommend a simple dietary screening questionnaire given early in the first trimester to help identify women with high-risk eating habits associated with GDM and providing individualized dietary feedback and advice. JAMA Netw Open. Moses RG, Barker M, Winter M, Petocz P, Brand-Miller JC. 2018;6(1):e000456. Change preparedness is high, as emotion is increased because of perceived risk but with the possibility of improved outcome with change. Tieu J, Shepherd E, Middleton P, Crowther CA. 2008;56:27-32. 2018;145:39-50. Teratology. Am J Obstet Gynecol. After 7 weeks on the diet, fasting glucose (p = 0.03) and FFAs (p = 0.06) decreased in those on the CHOICE diet, whereas fasting glucose increased in those on the low-carbohydrate diet (p = 0.03). Role of medical nutrition therapy in the management of gestational diabetes mellitus. Br J Clin Pharmacol. Aust N Z J Obstet Gynaecol. 2002;78(1):69-77.doi:10.1016/s0020-7292(02)00092-9Hughes RCE, Moore MP, Gullam JE, Mohamed K, Rowan J. Overweight and obesity among women with GDM complicate dietary management. Globally, the most widely used guideline for GWG is the Institute of Medicine (IOM) guideline [8] which recommends appropriate amount of weight gain per trimester depending on the pre-pregnancy BMI. Birth weight and its relation with medical nutrition therapy in gestational diabetes. 2017;2(2):CD009275. A lower carbohydrate and higher fat and protein intake may increase the risk of GDM in at-risk women [20]. The St Carlos study. Most clinicians start insulin as 0.5 to 1 unit/kg per day with 50% basal and 50% bolus. Oral Antihyperglycemic AgentsObstetricians tend to use 2 oral antihyperglycemic drugs— glyburide and metformin (Table 22,9-17)—in pregnancy, with no clear benefit from either. Cyclamates are not approved [11].Interventions to Prevent GDM - Probiotics and MyoinositolPreventing GDM could have several benefits such as reduction in the immediate adverse outcomes during pregnancy, a reduced risk of long-term sequelae, and a decrease in the economic burden to health care systems. 7th ed. High-fibre foods in a mixed meal can serve the same purpose as low-GI diets. To understand the difference between low-GI diets and high-fibre diets, 139 women at high risk of GDM (mean [SD] age: 34.7 [0.4] years and pre-pregnancy BMI: 25.2 [0.5] kg/m2) were randomly assigned to either a low-GI diet (GI target ~50) or a high-fibre, moderate-GI diet (target GI ~60) during 14-20 weeks of gestation. 2016;12(9):533-46. Barbour LA, Hernandez TL. The conventional focus so far has been to rigidly limit all types of carbohydrates; though it may help control glucose, it also fosters maternal anxiety and is an important barrier to adherence [1]. 2016;39(1):31-8. Muktabhant B, Lawrie TA, Lumbiganon P, Laopaiboon M. Maternal lipids and fetal overgrowth: making fat from fat. In conclusion, in women at high risk of developing GDM, the current evidence has showed that dietary advice, probiotics, and myoinositol supplementation might reduce the incidence of GDM. Interventions to Enhance Healthy Eating and Meal PlanningSystematic reviews studying 19 trials and comparing the effects of 10 different types of dietary advice for women with GDM found no conclusive evidence to show superiority of one approach or diet programme over others [37]. 190 gestational diabetes mellitus. Bethesda, MD: Institute of Medicine and National Research Council; 2013. Carpenter-Coustan compared with National Diabetes Data Group criteria for diagnosing gestational diabetes. Kapur K, Kapur A, Ramachandran S, Mohan V, Aravind SR, Badgandi M, et al. The American Diabetes Association (ADA) indicates that 70% to 85% of women have class A1 GD or diet-controlled GD. Pharmacoepidemiol Drug Saf. Most GDM guidelines of various professional organizations (Table 1) do not specify the amount of recommended fat intake; amongst those who do, there is a wide variation in recommended fat intake; amongst those who do, there is a wide variation in recommended fat intake; amongst those who do, there is a wide variation in recommended fat intake; amongst those who do, there is a wide variation in recommended fat intake; amongst those who do, there is a wide variation in recommended fat intake; amongst those who do, there is a wide variation in recommended fat intake; amongst those who do, there is a wide variation in recommended fat intake; amongst those who do, there is a wide variation in recommended fat intake; amongst those who do, there is a wide variation in recommended fat intake; amongst those who do, there is a wide variation in recommended fat intake; amongst those who do, there is a wide variation in recommended fat intake; amongst those who do, there is a wide variation in recommended fat intake; amongst those who do, there is a wide variation in recommended fat intake; amongst those who do, there is a wide variation in recommended fat intake; amongst those who do, there is a wide variation in recommended fat intake; amongst those who do, there is a wide variation in recommended fat intake; amongst those who do, there is a wide variation in recommended fat intake; amongst those who do, there is a wide variation in recommended fat intake; amongst those who do, there is a wide variation in recommended fat intake; amongst those who do, there is a wide variation in recommended fat intake; amongst those who do, there is a wide variation in recommended fat intake; amongst those who do, there is a wide variation in recommended fat intake; amongst those who do, there is a wide variation in recommended fat intake; amongst those who do, there is a wide variation in recommended fat intake; amongst those who do, there is a wide variation in recommended fat intake; amongst those who do, could help improve eating habits and better manage the pregnancy. Pregnancy provides an eminent window of opportunity for changing behaviour towards healthy eating and lifestyle and is considered a wonderful teachable moment for women and their families. randomized controlled clinical trials. Some recommend between 1,500 and 2,000 kcal/day and others a 30% caloric lowcarbohydrate diet (40% carbohydrate/25% fat/15% protein; n = 6) diet. Despite this, adherence to nutrition advice is often less than satisfactory. IDF Diabetes Voice. Are source and amount of fat and salt intake in the diet at large? Curr Diab Rep. Eslamian L. Akbari S. Marsoosi V. Jamal A. Tsirou E. Grammatikopoulou MG. Theodoridis X. Gkiouras K. Petalidou A. Taousani E. et al. Most fall in the range of 20-35% of daily EI. ProteinAdeguate protein intake during pregnancy is essential to prevent depletion of maternal stores and prevent muscle breakdown to supply for the foetal needs. No particular diet or dietary protocol is superior to another as shown in several comparative studies. Lauszus KS, et al. The control diet contained 45-55% carbohydrates, 15-20% protein, and 25-30% total fat while the DASH diet was rich in fruits, vegetables, whole grains, and low-fat dairy products and contained lower amounts of saturated fats, cholesterol, and refined grains with a total of 2,400 mg/day sodium. Olmedo-Reguena R, Gómez-Fernández J, Amezcua-Prieto C, Mozas-Moreno J, Khan KS, Jiménez-Moleón JJ. J Diabetol. Analysis of GDM excessive GWG [13]. In fact, in GDM, diets higher in unrefined/complex carbohydrates have been shown to effectively blunt post-prandial glycaemia [28, 29], reduce the need for insulin therapy [30], lower fasting LDL cholesterol levels [28, 31] and FFAs [28], and improve insulin sensitivity [32], HbA1C [31], and systolic blood pressure [31]. The role of low-GI diets in GDM has been extensively studied. doi:10.1016/j.ajog.2013.03.022Landi SN, Radke S, Boggess K, et al. Improved glucose tolerance in gestational diabetic women on a low fat, high unrefined carbohydrate diet. In a randomized study of women with GDM, CHO restriction (40% of total calories, compared to 60% complex CHO) was accompanied by 20% higher post-prandial FFAs [41]. It is therefore important that the fat content total and saturated fat of diets of women with GDM need to be moderated. Hernandez TL, Van Pelt RE, Anderson MA, Reece MS, Reynolds RM, de la Houssaye BA, et al. [19], carbohydrate restriction to

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