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Gestational Diabetes Mellitus — Risk Factors and Screening

By Rita Carey Rubin, MS, RD, CDE

The maternal and fetal complications of diabetes in pregnancy are well documented. Excessive fetal weight gain, fetal hyperinsulinemia, preeclampsia, and neonatal hypoglycemia are a few of the acute and potentially costly outcomes associated with the disease. Long-term risks include type 2 diabetes and obesity in offspring and postpartum maternal type 2 diabetes.

While there is consensus among healthcare professionals regarding the importance of maintaining tight glucose control in women with either gestational diabetes mellitus (GDM) or preexisting diabetes, controversy exists concerning the value of treating maternal hyperglycemia below blood glucose levels not diagnostic of overt disease.

This debate received renewed attention in 2010 when the International Association of Diabetes and Pregnancy Study Groups (IADPSG) recommended revisions to existing diagnostic criteria and screening protocols used to identify women with GDM. The revised screening guidelines would allow for earlier detection of maternal hyperglycemia and undiagnosed type 2 diabetes and would lower the diagnostic blood glucose thresholds used to diagnose GDM.

In 2011, the American Diabetes Association (ADA) revised its Standards of Medical Care in Diabetes to reflect these new recommendations. The ADA decided to revise its screening and diagnostic guidelines after considering the substantial evidence supporting the value of treating lower levels of hyperglycemia in pregnancy and also identifying women with previously undiagnosed type 2 diabetes.

As the new ADA recommendations are implemented by healthcare practitioners, dietitians may receive more frequent referrals to provide pregravid counseling on obesity or glucose intolerance as well as hyperglycemia in pregnancy and GDM. This CPE module will describe the current ADA Standards of Medical Care for Gestational Diabetes, the evidence supporting more inclusive diagnostic and screening protocols, the pathophysiology of gestational diabetes, and the risk factors for developing the disease.

Definition and Prevalence

GDM is defined as any degree of glucose intolerance, with onset or first recognition during pregnancy.[1] According to the 2011 statistics cited by the National Institutes of Health (NIH), gestational diabetes affects 2% to 10% of all pregnancies in the United States. The new diagnostic guidelines, if followed universally, could raise this number as high as 18%.[2]

Who Is at Risk?

Nonmodifiable risk factors for gestational diabetes include advanced maternal age (older than 35), a family history of type 2 diabetes, and a personal history of GDM.[3-5] According to Zhang and Ning, in a review of epidemiologic evidence of GDM risk factors, Asian, Hispanic, and Native American women have an increased risk of developing GDM over non-Hispanic white women.[4] Evidence supporting an increased risk for African American women is less conclusive.[4] Some evidence even suggests that short stature, especially combined with a BMI greater than 25, may be an additional nonmodifiable risk factor for GDM.[5,6]

Modifiable risk factors include BMI, dietary pattern, and level of physical activity.[3-5,7-9] Cigarette smoking has been identified as a potential risk factor, but research has not demonstrated a consistent, positive relationship between smoking and the development of GDM.[4] Obesity is the most commonly investigated modifiable risk factor with the most predictable findings. In fact, research has consistently supported a significant and positive linear correlation between levels of adiposity and the risk of developing GDM.[3,4,7]

Dietary Factors and GDM

Some studies have demonstrated a link between specific dietary habits during pregnancy and GDM risk. Although no concrete conclusions may be drawn from any of the studies regarding the role of specific dietary factors and the prevention or development of GDM, the associations observed are intriguing and important to note.

An analysis of data from the Pregnancy, Infection, and Nutrition Study (PIN) demonstrated an association between the development of both impaired glucose tolerance (IGT) and GDM with increased fat and lower carbohydrate intake during the second trimester of pregnancy.[8] The analysis of the PIN data also revealed that women who had a higher pregravid BMI (higher than 29) were more likely to develop GDM, as were women who were older (28 y $\pm$ 5.6 vs. 26 y $\pm$ 6.2). Women who developed IGT or GDM had a higher saturated fat intake in the second trimester than women who remained diabetes free. The top food sources of saturated fat reported were mayonnaise, cheese, whole milk, biscuits or muffins, and deep-fried potatoes.

In contrast to the above findings, a study by Wang et al found a reverse correlation between fat intake and GDM risk.[9] Variations in population size and type between the Wang and PIN studies are noteworthy and may explain the differing results. The Wang study was small, with only 171 participants, compared with 1,698 in the PIN study. Further, in the Wang study, all participants were Chinese, while the PIN study included only Caucasian and African American women.

As in the PIN study, the Wang study revealed that women with a higher BMI demonstrated a greater risk of developing IGT and GDM. These results are not comparable between the two studies, however, as Wang et al recorded participant's weight in the second trimester, not prior to conception, as in the PIN study.

The main source of fat in the diets of the Wang study participants was soybean oil, a polyunsaturated fat. Researchers found that the intake of a higher percentage of calories from soybean oil correlated with a lower incidence of IGT and GDM, independent of body weight.

Accordingly, Wang et al suggest that polyunsaturated fats may have a protective effect against GDM in the studied population.

There are many other studies that offer interesting but conflicting evidence regarding the impact of dietary fat intake during pregnancy and the development of GDM or IGT. For example, Bo et al found that a small sample of pregnant Caucasian women with either GDM or IGT tended to be older (35 or older), overweight, or obese and had diets higher in saturated fat than women without glucose abnormalities.[5] The Bo study also revealed that saturated fat played an independent role in the development of GDM in the studied population. In other words, women without conventional risk factors for GDM (BMI less than 25, younger than 35, and no known first-degree relatives with diabetes) had a greater risk of developing IGT or GDM if their diets were high in saturated fat during pregnancy.

In contrast to the findings of the Bo study, a study by Radesky et al found no association between the intake of saturated fat, polyunsaturated fat, and trans fats in the first trimester diets of 1,733 women and the development of IGT or GDM at 26 to 28 weeks. The authors of this study found that prepregnancy BMI was more predictive of glucose abnormalities in the third trimester than specific nutrient intakes during early pregnancy.10

Although no specific dietary characteristics have definitively been identified as risk factors for GDM, this research suggests that a diet containing excessive amounts of saturated fat may trigger development of the disease. On the other hand, prepregnancy BMI seems to be a strong predictive risk factor and is likely one of the most important considerations when screening women for GDM or IGT risk.

Physical Activity and GDM

Moderate physical activity is known to increase insulin sensitivity in nonpregnant individuals and has been shown to lower the risk of developing type 2 diabetes in middle-age and elderly men, Native Americans, and women, independent of BMI.[11-13] Individuals with diabetes regularly note the effects of exercise in lowering blood glucose levels for many hours afterward. In fact, studies in rats indicate that insulin sensitivity may be improved and glucose levels may be reduced for up to 18 hours after exercise.[14]

In their review of diet and lifestyle factors influencing the development of GDM, Zhang and Ning note several studies that demonstrate a positive correlation between exercise before and/or during pregnancy and reduced GDM risk.[4] For example, women in the Nurses' Health Study who reported the greatest amount of regular exercise before pregnancy had a 20% reduced risk of developing GDM.[15]

Similarly, a small case-control study found that the type, intensity, and frequency of recreational exercise performed before and during the first 20 weeks of pregnancy had a direct, linear relationship with the reduction in GDM risk.[16] In this study of approximately 500 pregnant women, those who spent the most time exercising and with the greatest intensity reduced risk of GDM by up to 78%.

Obesity and GDM

Pregravid BMI is a major determinant of pregnancy outcome. In fact, an elevated BMI is associated with an increased risk of preeclampsia, GDM, gestational hypertension, large-for-gestational-age (LGA) births, and Caesarean delivery. In a review of research on maternal obesity and pregnancy outcomes, Nelson, Matthews, and Poston detailed maternal and fetal metabolic changes associated with obesity as well as the different risks associated with prepregnancy obesity, gestational weight gain (GWG), and LGA births (weight and length greater than 90% for gestational age after correcting for neonatal sex and ethnicity).[17]

GWG is a normal function of pregnancy, with both subcutaneous and visceral fat accumulating in the body. Visceral fat accretion during pregnancy is associated with the same metabolic changes that occur in nonpregnant women: increased blood pressure, decreased insulin sensitivity, glucose intolerance, and increased plasma lipids. Per Nelson, Matthews, and Poston, the most consistent negative outcome for excessive GWG is postdelivery weight retention. In a study of more than 150,000 Swedish women, weight retention of 3 kg/m^2 after the first pregnancy significantly increased the risk of LGA birth, preeclampsia, GDM, hypertension, and Caesarean delivery in subsequent pregnancies.[18] However, GWG alone has not been found to be directly associated with an increased risk of GDM. Prepregnancy BMI is more strongly associated with GDM risk.[17]

In obese women, the normal changes in plasma lipids and glucose metabolism that occur during pregnancy are amplified.[17] Triglyceride levels are higher in obese, pregnant women and small, dense LDL particles are more susceptible to oxidation, a classic contributor to endothelial dysfunction and atherosclerosis. These lipid changes are also thought to be direct contributors to preeclampsia. Insulin sensitivity in late normal pregnancies is reduced by 50% to 70%, but in obese pregnancies, insulin sensitivity is even more severely impaired. Obesity-related insulin resistance exaggerates the normal increases in glucose, free fatty acid, and amino acid levels that cross the placenta to the fetus. This increased availability of nutrients is thought to contribute significantly to macrosomia (birth weight of 4 kg or more) and LGA births.

The 2008 ***New England Journal of Medicine*** Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study demonstrated the important influence of maternal glycemia and birth weight above the 90th percentile. In the HAPO Study, maternal glucose levels were linearly related to infant adiposity, which in turn was directly related to infant hyperinsulinemia. Higher birth weight is also strongly associated with higher BMI in childhood and the risk of overweight or obesity later in life.[19]

Long-Term Complications of GDM

According to the NIH, women with GDM have a 35% to 60% chance of developing type 2 diabetes within 20 years.[2] As determined by the HAPO and other studies, women with GDM are at higher risk of giving birth to large infants.20 Infants who are born LGA are prone to develop the metabolic syndrome, obesity, diabetes, and cardiovascular disease later in life, and some evidence suggests they may be at greater risk for developing childhood leukemia.[19,21,22]

New Data Supporting Intensive GDM Screening and Treatment

The results of three randomized interventional trials demonstrate improved pregnancy outcomes with routine screening for and treatment of GDM. The largest of these trials, the previously mentioned HAPO Study, utilized data from more than 23,000 participants in nine countries to determine whether maternal hyperglycemia less severe than overt diabetes (ie, maternal glucose intolerance) negatively affects pregnancy. The outcomes tracked in this study are listed in Table 1 below.

Results indicate positive associations between the levels of maternal hyperglycemia and all primary and secondary study outcomes, with the strongest associations occurring between levels of hyperglycemia, birth weight, and serum cord-blood C-peptide levels. (Elevated C-peptide levels indicate fetal hyperinsulinemia.) In fact, with increasing maternal glucose levels, the frequency of each primary outcome increased, although less so for clinical neonatal hypoglycemia than for the other outcomes. These associations remained significant after adjusting for potential confounders (maternal weight and age, caregiver bias, and other medical complications).

Two smaller studies published in ***The New England Journal of Medicine***, the Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) trial (2005) and a randomized trial funded by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (2009), also demonstrated improved maternal and neonatal outcomes with screening for and treatment of GDM.

In these studies (each with approximately 1,000 participants), significantly fewer infants in the groups treated for GDM were LGA and significantly fewer had macrosomia. Maternal weight gain was lower in the treatment groups, and fewer women receiving treatment had preeclampsia. In addition, the women in the treatment groups made more prenatal visits to the medical clinic for diabetes education and treatment. Moreover, in the ACHOIS trial, these women also required fewer medical visits after their infants were born. Also noteworthy, Caesarean section rates were either the same between study groups or lower in the groups of women treated for GDM.

IADPSG Recommendations

The IADPSG formed in 1998 to facilitate research and education about diabetes during pregnancy and enhance the quality and standardization of care in the field.[23] The group met in 2008 to review the results of several published and unpublished studies examining links between maternal hyperglycemia and adverse pregnancy outcomes. Conference attendees then held additional meetings to consider the clinical importance of these findings.

The IADPSG recommendations are based on the results of the HAPO Study and other studies that conclusively demonstrated a positive, linear relationship between levels of maternal hyperglycemia and negative pregnancy outcomes. Due to the high quality of trial procedures and the analysis of the HAPO Study results, the data from that study were used as the basis for the new GDM diagnostic thresholds recommended in the IADPSG report.

The IADPSG suggests a new strategy for the detection and diagnosis of diabetes and hyperglycemic disorders in pregnancy and describes the strategy in two phases. The first phase deals with identifying women with undiagnosed, preexisting type 2 diabetes. The group recommends compulsory screening for diabetes in all pregnant women or, if more economically or logistically feasible, all women in high-risk populations (those with a high prevalence of type 2 diabetes). The second phase is a 75-g oral glucose tolerance test (OGTT) performed at 24 to 28 weeks in all women not previously found to have either prepregnancy diabetes or GDM.

2011 ADA Standards of Medical Care in Diabetes

• Screen for type 2 diabetes at the first prenatal visit in those with risk factors.

• In pregnant women without diagnosed diabetes, screen for gestational diabetes at 24 to 28 weeks of gestation using a 75-g two-hour OGTT and diagnostic cutoff points recommended by the IADPSG (see Table 2 below).

• Screen women with GDM for type 2 diabetes at six to 12 weeks postpartum.

• Conduct lifelong diabetes screening for women with a history of GDM at least every three years.

These revised standards, published in the January 2011 issue of ***Diabetes Care***, reflect concern regarding negative maternal and fetal outcomes from all levels of hyperglycemia during pregnancy and also recognize the larger implications of the ongoing diabetes epidemic in women of childbearing age. Per the ADA, “As the ongoing epidemic of obesity and diabetes has led to more type 2 diabetes in women of childbearing age, the number of pregnant women with undiagnosed type 2 diabetes has increased. Because of this, it is reasonable to screen women with risk factors for type 2 diabetes … at their initial prenatal visit, using standard diagnostic criteria. Women with diabetes found at this visit should receive a diagnosis of overt, not gestational diabetes.”

In other words, after considering the IADPSG findings, the ADA concluded that it is a reasonable and good practice to adopt protocols that identify a greater number of pregnant women with preexisting diabetes as well as impaired carbohydrate metabolism (with glucose levels not previously indicative of GDM).

Clinical Implications

According to Boyd Metzger, corresponding author of the IADPSG, the major clinical implication of the new screening and diagnostic protocols recommended for GDM will be the ability to identify the risk of adverse pregnancy outcomes with one abnormal glucose value instead of two. The authors of the IADPSG paper note that these new diagnostic criteria, if universally practiced, will likely increase the frequency of hyperglycemic disorders diagnosed in pregnancy. They also note that an increased incidence of GDM or IGT in pregnancy is consistent with the increased prevalence of obesity and diabetes in the general population of childbearing adults. The authors recommend clinical studies to determine the most cost-effective way to utilize the new criteria.

In its standards of care paper, the ADA concedes that no data currently exist concerning cost-effectiveness or pregnancy outcomes in women diagnosed with GDM using the new criteria. They do note, however, that most cases of mild GDM or IGT are successfully treated with diet and lifestyle therapy alone and do not require more costly interventions.

—Rita Carey Rubin, MS, RD, CDE is a dietitian practicing in northern Arizona.

Table 1: HAPO Study Primary and Secondary Outcomes[24]

Primary Study Outcomes	**Secondary Study Outcomes**
Birth weight above the 90th percentile for gestational age	Premature delivery
Cesarean delivery	Shoulder dystocia or birth injury
Neonatal hypoglycemia	Need to intensive neonatal care
Cord-blood serum C-peptide levels above the 90th percentile	Hyperbilirubinemia
	Preeclampsia

Table 2: Diagnostic Criteria Recommended by the IADPSG[23]

To Diagnose GDM	
	Glucose Level Diagnostic of Disease
Fasting plasma glucose	92 mg/dL
OGTT 1-hour plasma glucose	180 mg/dL
OGTT 2-hour plasma glucose	153 mg/dL

To Diagnose Overt Diabetes in Pregnancy	
	Glucose Level Diagnostic of Disease
Fasting plasma glucose	≥ 126 mg/dL
Random plasma glucose	≥ 200 mg/dL + confirmation
Hemoglobin A1c	≥ 6.5%

References

1. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. ***Diabetes Care***. 1997;20(7):1183-1197.

2. National diabetes statistics, 2011. National Diabetes Information Clearinghouse website. http://diabetes.niddk.nih.gov/DM/PUBS/statistics/#Gestational. Accessed January 5, 2012.

3. Solomon CG, Willett WC, Carey VJ, et al. A prospective study of pregravid determinants of gestational diabetes mellitus. ***JAMA***. 1997;278(13):1078-1083.

4. Zhang C, Ning Y. Effect of dietary and lifestyle factors on the risk of gestational diabetes: review of epidemiologic evidence. ***Am J Clin Nutr***. 2011;94(Suppl):1975S-1979S.

5. Bo S, Menato G, Lezo A, et al. Dietary fat and gestational hyperglycaemia. ***Diabetologia***. 2001;44(18):972-978.

6. Branchtein L, Schmidt MI, Matos MC, Yamashita T, Pousada JM, Duncan BB. Short stature and gestational diabetes in Brazil. Brazilian Gestational Diabetes Study Group. ***Diabetologia***. 2000;43(7):848-851.

7. Chu SY, Callaghan WM, Kim SY, et al. Maternal obesity and risk of gestational diabetes mellitus. ***Diabetes Care***. 2007;30(8):2070-2076.

8. Saldana TM, Siega-Riz AM, Adair LS. Effect of macronutrient intake on the development of glucose intolerance during pregnancy. ***Am J Clin Nutr***. 2004;79(3):479-486.

9. Wang Y, Storlien LH, Jenkins AB, et al. Dietary variables and glucose tolerance in pregnancy. ***Diabetes Care***. 2000;23(4):460-464.

10. Radesky JS, Oken E, Rifas-Shiman SL, Kleinman KP, Rich-Edwards JW, Gillman MW. Diet during early pregnancy and the development of gestational diabetes. ***Paediatr Perinat Epidmiol***. 2008;22(1):47-59.

11. Fretts AM, Howard BV, Kriska AM, et al. Physical activity and incident diabetes in American Indians. The Strong Heart Study. ***Am J Epidemiol***. 2009;170(5):632-639.

12. Helmrich SP, Ragland DR, Leung RW, Paffenbarger RS Jr. Physical activity and reduced occurrence of non-insulin-dependent diabetes mellitus. ***N Engl J Med***. 1991;325:147-152.

13. Hu FB, Sigal RJ, Rich-Edwards JW, et al. Walking compared with vigorous physical activity and risk of type 2 diabetes in women: a prospective study. ***JAMA***. 1999;282(15):1433-1439.

14. Holloszy JO. Exercise-induced increase in muscle insulin sensitivity. ***J Appl Physiol***. 2005;99(1):338-343.

15. Zhang C, Solomon CG, Manson JE, Hu FB. A prospective study of pregravid physical activity and sedentary behaviors in relation to the risk for gestational diabetes mellitus. ***Arch Intern Med***. 2006;166(5):543-548.

16. Dempsey JC, Butler CL, Sorensen TK, et al. A case-control study of maternal recreational physical activity and risk of gestational diabetes mellitus. ***Diabetes Res Clin Pract***. 2004;66(2):203-215.

17. Nelson SM, Matthews P, Poston L. Maternal metabolism and obesity: modifiable determinants of pregnancy outcome. ***Hum Reprod Update***. 2010;16(3):255-275.

18. Villamor E, Cnattingius S. Interpregnancy weight change and risk of adverse pregnancy outcomes: a population-based study. ***Lancet***. 2006;368(9542):1164-1170.

19. Boney CM, Verma A, Tucker R, Vohr BR. Metabolic syndrome in childhood: association with birth weight, maternal obesity, and gestational diabetes mellitus. ***Pediatrics***. 2005;115(3):290-296.

20. Kerenyi Z, Tamas G, Kivimaki M, et al. Maternal glycemia and risk of large-for-gestational-age babies in a population-based screening. ***Diabetes Care***. 2009;32(12):2200-2205.

21. Ross JA. High birthweight and cancer: evidence and implications. ***Cancer Epidemiol Biomarkers Prev***. 2006;15:1-2.

22. Kleiser C, Rosario AS, Mensink GBM, Prinz-Langenohl R, Kurth B. Potential determinants of obesity among children and adolescents in Germany: results from the cross-sectional KiGGS study. ***BMC Public Health***. 2009;9:46.

23. International Association of Diabetes and Pregnancy Study Groups Consensus Panel, Metzger BE, Gabbe SG, 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):676-682.

24. HAPO Study Cooperative Research Group, Metzger BE, Lowe LP, et al. Hyperglycemia and adverse pregnancy outcomes. ***N Engl J Med***. 2008;358(19):1991-2002.

Examination

1. Potential effects of gestational diabetes on pregnancy outcome include:
A. Caesarian birth.
B. preeclampsia.
C. excessive fetal weight gain.
D. All of the above

2. New screening protocols and diagnostic criteria for gestational diabetes may result in:
A. more women diagnosed with gestational diabetes.
B. more women diagnosed with type 2 diabetes.
C. greater medical costs.
D. All of the above

3. The single most important modifiable risk factor for developing gestational diabetes is:
A. intake of dietary fat during pregnancy.
B. physical activity level.
C. pregravid BMI.
D. fluid intake.

4. The Hyperglycemia and Adverse Pregnancy Outcome study demonstrated a direct, linear correlation between levels of maternal hyperglycemia and the incidence of large-for-gestational-age infants, neonatal hyperinsulinemia, and Caesarian section.
A. True
B. False

5. A woman who develops gestational diabetes in her first pregnancy is 75% more likely to develop type 2 diabetes within 10 years than a woman who does not develop gestational diabetes.
A. True
B. False

6. The new diagnostic criteria for gestational diabetes suggested by the International Association of Diabetes and Pregnancy Study Groups (IADPSG) include the following glucose thresholds:
A. Fasting glucose of 100 mg/dL
B. 1-hour oral glucose tolerance test (OGTT) of 153 mg/dL
C. 2-hour OGTT of 153 mg/dL on two occasions
D. 1-hour OGTT of 180 mg/dL

7. The IADPSG recommends screening all pregnant women for preexisting diabetes because:
A. the incidence of type 1 diabetes in women of childbearing age is on the rise.
B. glucose intolerance begins to show up in the first trimester of pregnancy.

C. the obesity epidemic has resulted in more cases of type 2 diabetes in women of childbearing age.
D. All of the above

8. Caucasian women are at greater risk of developing gestational diabetes than women of other ethnic groups.
A. True
B. False

9. An increased incidence of gestational diabetes may eventually lead to an increased incidence of childhood obesity in the United States.
A. True
B. False

10. Excessive gestational weight gain may increase the risk of developing gestational diabetes during subsequent pregnancies if the mother:
A. does not engage in physical activity before the next pregnancy.
B. does not lose the weight she gained before the next pregnancy.
C. consumes a diet high in saturated fat before the next pregnancy.