

# Managing Diabetes in Pregnancy

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This program is supported by an educational grant from Novo Nordisk Inc. It has been approved by the American Association of Diabetes Educators (AADE) for pharmacists, nurses, and dietitians.

*Managing Diabetes in Pregnancy* provides information on preconception care, treatment, and follow-up for women with type 1 or type 2 diabetes prior to pregnancy and for those who develop gestational diabetes during pregnancy. It also includes information on the diagnosis of gestational diabetes.

# Carol Homko, RN, PhD, CDE



Associate Research Professor  
Department of Medicine Division of Endocrinology/Metabolism/Diabetes  
Temple University School of Medicine  
Philadelphia, PA

The following program is a presentation by Carol Homko.

Dr. Homko is a nurse and certified diabetes educator, with almost 30 years of experience in diabetes education and management. She established the Diabetes and Pregnancy Program at Temple University Hospital in 1991 and continues to maintain an active clinical practice there. At the present time, Dr. Homko is an Associate Research Professor in the Department of Medicine, Division of Endocrinology/Metabolism/Diabetes at the Temple University School of Medicine.

For the past fifteen years, her primary research has focused on gestational diabetes mellitus and pregnancies complicated by pre-existing diabetes. She has published widely in peer-reviewed journals and has authored multiple chapters on the management of pregnancies complicated by diabetes including AADE's Core Curriculum for Diabetes Education (4th edition) and a contributor to AADE's Diabetes Education Review Guide. Dr. Homko lectures frequently to local, national, and international audiences of health professionals. She is actively involved with the American Diabetes Association and the American Association of Diabetes Educators at both the local and national levels. Dr. Homko is a past chair of the Pregnancy/Reproductive Health AADE Specialty Practice Group.

## Learning Objectives

- Explain changes in metabolism during pregnancy
- Review the prevalence and impact of diabetes in pregnant women
- Discuss preconception care in women with diabetes
- Describe the similarities and differences in the management of preexisting diabetes and gestational diabetes
- Identify potential fetal complications associated with maternal diabetes

The goal of this program is to provide information and guidance on the management of diabetes (both preexisting and gestational) before, during, and after pregnancy.

The objectives are to:

- Explain changes in metabolism during pregnancy
- Review the prevalence and impact of diabetes in pregnant women
- Discuss preconception care in women with diabetes
- Describe the similarities and differences in the management of preexisting diabetes and gestational diabetes
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# Metabolic Changes During Normal Pregnancy

## First trimester

- Provision of glucose to fetus resulting in
  - Decreased fasting maternal glucose levels
  - Accelerated ketogenesis
  - Lower concentrations of most amino acids

## Second and third trimesters

- Insulin resistance, due in part to increased levels of circulating hormones
  - Human placental lactogen (HPL)
  - Estrogen
  - Progesterone
  - Cortisol
  - Prolactin
- Possible tripling of plasma insulin levels by third trimester

Many metabolic changes take place during normal pregnancy.

The following changes in metabolism take place during the first trimester.

- The provision of glucose and gluconeogenic substrate to the fetus results in a drop in maternal glucose levels to 55 to 65 mg/dL in the fasting state. These levels are well below those seen in nonpregnant fasting glycemia.
- Plasma ketone concentrations are higher than usual and free fatty acid levels are elevated after an overnight fast. Thus, pregnancy simulates a state of “accelerated starvation,” leading to the increased use of alternate fuels for maternal metabolism while glucose is spared for fetal consumption.
- Amino acids are actively transported to the fetal circulation, resulting in lower circulating concentrations of most amino acids.

During the second and third trimesters, circulating insulin levels are increased, partly because of accelerated hormonal activity counteracts insulin action. During late pregnancy, there are increases in the levels of many hormones, including human placental lactogen (HPL), estrogen, progesterone, cortisol, and prolactin.

To maintain euglycemia, plasma insulin levels may triple by the third trimester.

## Metabolic Changes During Normal Pregnancy (cont'd)

### Late Pregnancy

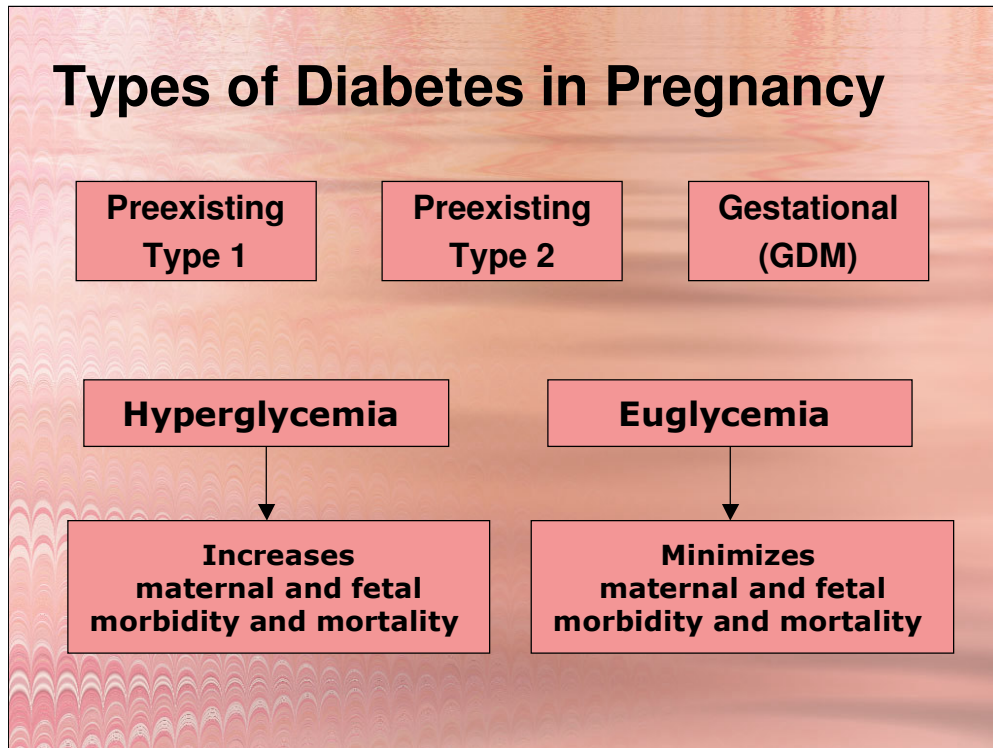
- Food ingestion results in higher plasma glucose concentrations and longer periods of elevated concentrations
  - Changes enhance transplacental delivery of glucose to fetus and promote fetal growth
  - Insulin requirements increase 2- to 3-fold
- Maternal insulin and glucagon do not cross placenta

During late pregnancy, food ingestion results in higher plasma glucose concentrations and more prolonged periods of elevated glucose concentrations. These changes enhance transplacental glucose delivery to the fetus and promote fetal growth.

Insulin requirements increase 2- to 3-fold during late pregnancy.

Maternal insulin and glucagon do not cross the placenta.

## Types of Diabetes in Pregnancy



The 3 major types of diabetes that may complicate pregnancy are preexisting type 1 diabetes, preexisting type 2 diabetes, and gestational diabetes mellitus (GDM).

- Preexisting type 1 diabetes is characterized by autoimmune destruction of  $\beta$ -cells, resulting in virtually absolute insulin deficiency.
- Preexisting type 2 diabetes is a heterogeneous metabolic dysfunction involving insulin resistance and defects in insulin secretion.
- GDM is carbohydrate intolerance of variable severity with onset or first recognition during pregnancy.

The population of women with GDM includes individuals who may have had type 2 diabetes prior to pregnancy but who are first diagnosed during pregnancy. Approximately 2% of women of childbearing age in the United States have undiagnosed type 2 diabetes. Forty percent to 60% of women diagnosed with GDM will develop type 2 diabetes within the next 5 to 15 years.

Unless glucose levels are well controlled, pregnancy complicated by diabetes is associated with significantly increased risks of maternal and fetal morbidity and mortality. Maintaining euglycemia can minimize maternal and fetal complications in all types of diabetes.

During pregnancy, maternal hypertension, dyslipidemia, and other comorbidities should also be managed.

## Prevalence and Impact of Preexisting Diabetes

- Diabetes is the most prevalent chronic disease in pregnant women
- Preexisting diabetes
  - Complicates about 2%–5% of all pregnancies in the US
  - Unplanned pregnancies in two thirds of women
  - Increasing prevalence of type 2 diabetes
  - Declining infant mortality rates in type 1 diabetes
  - Major congenital anomalies the leading cause of infant morbidity and mortality

Diabetes is the most prevalent chronic disease in pregnancy. Preexisting type 1 or type 2 diabetes complicates an estimated 2% to 5% of pregnancies in the United States. About two thirds of the pregnancies in women with preexisting diabetes are unplanned—a situation that increases the risk for complications in the mother and the infant. Today, about 34% of pregnant women with preexisting diabetes have type 1 diabetes, but the prevalence of type 2 diabetes in this population is steadily rising as the maternal population becomes older and heavier.

Although type 1 diabetes was formerly associated with very high infant mortality rates, rates had declined from 25% in the 1960s to 2% by the 1980s. This level, which persists to the present day, is similar to the infant mortality rate in women without diabetes. Among pregnancies complicated by preexisting type 1 or type 2 diabetes, major congenital anomalies are still the leading cause of morbidity and mortality. Congenital anomalies account for 40% to 50% of fetal deaths and occur in 6% to 12% of infants born to women with diabetes. The risk of congenital anomalies ranges from 2% to 5% when A1C is moderately elevated (7.0%–9.0%) and from 20%–40% when A1C is markedly elevated (>10.0%–14.4%).

## Improved Care = Improved Outcomes in Preexisting Diabetes

- Optimal metabolic control before and during pregnancy
- Advances in biochemical and electronic monitoring techniques
- Multidisciplinary team approach
  - Patient
  - Primary care physician or endocrinologist
  - Obstetrician/gynecologist
  - Certified diabetes educator
  - Registered nurse
  - Registered dietitian
  - Registered pharmacist
  - Social worker

In women with preexisting diabetes, optimal metabolic control before and during pregnancy is essential for a successful outcome, including a minimized risk of fetal malformations and neonatal complications.

Advances in biochemical and electronic monitoring techniques have markedly improved maternal and fetal care and well-being in pregnancy complicated by diabetes. Reduction in fetal mortality is due in part to the improved control of diabetes achieved with intensified insulin therapy protocols, modern methods of fetal monitoring, and the widespread availability of neonatal intensive care units.

A team approach to care that reinforces the importance of planning future pregnancies, encourages optimal blood glucose control before and during pregnancy, manages other comorbidities such as hypertension and dyslipidemia, promotes healthy lifestyle behavior changes, and includes the patient in all aspects of care is more likely to achieve desired results and favorable outcomes for both mother and child. In addition to the patient, team members may include the primary care physician or endocrinologist, obstetrician/gynecologist knowledgeable about diabetes and pregnancy, certified diabetes educator, registered nurse, registered dietitian, registered pharmacist specializing in diabetes, and social worker.

# Diabetes Care Before and During Pregnancy: Preexisting Diabetes

Preconception	Pregnancy	Labor and Delivery
Planning/contraception Evaluate for potential contraindications to pregnancy Counseling regarding potential complications Target A1C as close to normal as possible without significant hypoglycemia Type 2: switch to insulin Discontinue ACE inhibitors for hypertension and cholesterol medications	A1C <6.0 Nutrition and weight management Fetal monitoring Maternal complications monitoring	Fetal monitoring Glucose/insulin adjustments Postpartum glucose management Postpartum meal plan adjustment

ACE = angiotensin-converting enzyme.

Every woman with preexisting type 1 or type 2 diabetes requires preconception planning. The patient should be evaluated for the presence of potential contraindications to pregnancy and should receive counseling concerning potential maternal and fetal complications. To minimize the risk of complications, target A1C as close to normal as possible without significant hypoglycemia.

Patients with type 2 diabetes should transition from oral glucose-lowering agents to insulin prior to conception. Because angiotensin-converting enzyme (ACE) inhibitors are associated with neonatal renal failure, they should be discontinued as soon as pregnancy is detected and the patient switched to an antihypertensive medication demonstrated to be safe during pregnancy. Other medications whose use is contraindicated or not recommended during pregnancy include statins (eg, simvastatin) and angiotensin receptor blockers (eg, losartan).

During pregnancy, management focuses on maintaining maternal euglycemia to maximize chances for a positive outcome. Management includes blood glucose monitoring, nutrition and weight management, adjustment of insulin administration, and fetal monitoring. Potential maternal complications (eg, preeclampsia) should be monitored.

Goals during labor and delivery are to provide adequate carbohydrate intake to meet energy requirements and maintain maternal euglycemia. Postpartum, the woman's glucose control should be followed closely to reestablish her baseline insulin requirement or some patients may go back to their oral agents if not breastfeeding.

## Preconception Counseling and Care: Preexisting Diabetes

- Preconception counseling should continue from puberty through menopause
- Key elements of preconception counseling
  - Discuss readiness for pregnancy and possible risks
  - Assess self-management skills
  - Provide diabetes education for the woman and significant other (eg, glycemic control, nutrition)
- Preconception care should begin at least 3–6 months before conception

Because two thirds of pregnancies in women with type 1 or type 2 diabetes are unplanned, the American Diabetes Association (ADA) advises that preconception counseling begin at the onset of puberty and continue until menopause.

Elements of preconception counseling usually include:

- Reviewing the benefits of prepregnancy planning and contraception
- Discussing physiological and psychological readiness for pregnancy and possible risks
- Reinforcing the importance of good glycemic control prior to discontinuation of contraception
- Identifying any diabetes-related complications
- Referring the patient for obstetric evaluation
- Assessing self-management skills, including blood glucose monitoring and insulin injection techniques
- Providing diabetes education for the woman and her significant other
- Providing nutrition counseling (eg, meal planning, weight gain management, addition of protein, folic acid supplementation, taking other vitamin or mineral supplements)
- Reviewing current medications (including vitamins and herbal supplements)

Preconception care should begin at least 3 to 6 months before conception since many birth defects originate during the first trimester. Poorly controlled diabetes in the early weeks of pregnancy significantly increases the risk for first-trimester spontaneous abortions or delivering an infant with a major anomaly. In a recent British study in women with type 1 diabetes, the combined rate of major congenital anomalies, stillbirth, and neonatal death was 2.9% in women who received prepregnancy care and 10.2% in women who did not. Rates of delivery before 34 weeks' gestation were 5.0% in women who received preconception care and 14.2% in those who did not.

## Preconception Assessment: Preexisting Diabetes

- |   |   |
|---|---|
| <input type="checkbox"/> History and physical   | <input type="checkbox"/> Retinal exam                                   |
| <input type="checkbox"/> Laboratory evaluations | <input type="checkbox"/> Special studies (if indicated)                 |
| – A1C   | – 24-hr urine for creatinine clearance, total protein, microalbuminuria |
| – Urinalysis and culture                        | – EKG   |
| – Random urine for albumin-to-creatinine ratio  | – Neuropathy testing  |
| – ALT/AST levels                                |   |
| – Thyroid panel                                 |   |
| – Blood lipids                                  |   |

ALT = alanine aminotransferase; AST = aspartate aminotransferase; EKG = electrocardiogram

A preconception assessment of a woman with preexisting diabetes should start with a detailed medical history and physical examination that includes:

- Type of diabetes, age of onset, duration, and course of disease
- History of acute and chronic complications
- Current regimen with attention to routine insulin doses (if applicable), meal plan, exercise, hypoglycemia unawareness, self-monitoring of blood glucose (SMBG)
- Other medical problems, especially hypertension and dyslipidemia
- Obstetric history with attention to infertility problems and pregnancy complications
- All medications, including vitamins and herbal supplements
- Identification of support system (family and work environment)

An ophthalmologist should perform a retinal exam through a dilated pupil.

Laboratory evaluations should include:

- A1C to evaluate overall glucose control
- Urinalysis and culture to rule out infection
- Random urine test to determine albumin-to-creatinine ratio
- Alanine aminotransferase/aspartate aminotransferase levels to assess liver function
- Thyroid panel
- Blood lipids

Special studies may be indicated to assess severity if complications are present or identified in other tests:

- Electrocardiogram
- Neuropathy testing
- 24-hr urine collection for creatinine clearance, total protein, and microalbuminuria

## Contraindications to Pregnancy: Preexisting Diabetes

### □ Absolute

- Ischemic heart disease
- Active proliferative retinopathy

### □ Relative

- Renal insufficiency
  - Serum creatinine >2 mg/dL and/or creatinine clearance <50 mL/min
  - Blood pressure >130/80 mm Hg despite treatment
- Severe gastroenteropathy

There are absolute and relative contraindications to pregnancy for women with preexisting diabetes.

Absolute contraindications include ischemic heart disease and active proliferative retinopathy. The risk of maternal mortality is high in women with ischemic heart disease. If significant proliferative retinopathy is present, the woman may be advised to delay the pregnancy until treatment can stabilize the condition. Background retinopathy that occurs during pregnancy usually regresses after delivery.

Relative contraindications to pregnancy include renal insufficiency and severe gastroenteropathy. If significant renal disease is present, as validated by serum creatinine >2 mg/dL and/or creatinine clearance <50 mL/min, the woman must be warned about the high risk of infant morbidity and mortality associated with this complication. Significant proteinuria (>2 g/24 hr), when accompanied by hypertension, indicates significant risk.

When blood pressure measures between 130/80 and 140/90 mm Hg, therapeutic lifestyle changes are usually recommended. Hypertension treatment is initiated when blood pressure measures >140/90 mm Hg. During pregnancy and in the presence of renal insufficiency, blood pressure should be maintained at <130/80 mm Hg. ACE inhibitors should be discontinued and replaced with other antihypertensive medications, since this class of antihypertensive medication may cause genitourinary tract anomalies in the fetus.

Severe gastroenteropathy is a relative contraindication because metabolic control and nutrition for both the woman and her developing baby are very difficult to maintain with this complication.

## Check Point

### The correct statement about preexisting diabetes in pregnancy is:

- a) Outcomes have improved in women with type 2 diabetes and worsened in those with type 1 diabetes.
- b) An absolute contraindication to pregnancy is renal insufficiency.
- c) About one third of pregnancies in women with preexisting diabetes are unplanned.
- d) Preconception care should begin 3 to 6 months before conception.

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## Medical Management Strategy: Preexisting Diabetes

- Determined by patient and healthcare team
- Plan for glucose control
  - MNT, physical activity, medication (if necessary)
  - SMBG, ketones, food intake, weight gain
  - Treatment of hyperglycemia and hypoglycemia
- Monitoring maternal and fetal well-being
- Assessment of psychosocial and financial well-being

MNT = medical nutrition therapy.

A woman with preexisting diabetes and her healthcare providers should work as a team to determine the optimal medical management strategy. This plan should include preconception and postpartum care as well as care during pregnancy.

They should develop a plan for glucose control that includes medical nutrition therapy (MNT), physical activity, and, if necessary, medication.

The strategy should incorporate SMBG, ketones, food intake, and weight gain, as well as approaches for treating hyperglycemia and hypoglycemia.

The team should also monitor maternal and fetal well-being and assess maternal psychosocial and financial well-being.

## Glycemic Goals in Pregnancy

	Blood Glucose Value (mg/dL)
Premeal, bedtime, and overnight	60–99
Peak postprandial	100–129
Mean daily	<110

In pregnant women without diabetes, maternal plasma glucose remains around 100 mg/dL, from fasting levels of 60 mg/dL to postprandial levels of 120 mg/dL.

According to the ADA, optimal glycemic goals throughout pregnancy are:

- Premeal, bedtime, and overnight glucose 60 to 99 mg/dL
- Peak postprandial glucose 100 to 129 mg/dL
- Mean daily glucose <110 mg/dL

Higher glucose targets may be used for women with hypoglycemia unawareness or the inability to cope with intensified management.

## Monitoring Glycemic Control: Preexisting Diabetes

- Perform SMBG
  - Premeal and postprandial as well as bedtime monitoring recommended, especially with MDI or CSII therapy
  - Middle-of-night monitoring if nighttime hypoglycemia suspected
  - Precise monitoring schedules to be individualized
- Record food intake along with SMBG results
- Test A1C monthly until target levels <6.0 are achieved, then every 2–3 months
- Monitor ketones during illness, when blood glucose is >200 mg/dL, or when regular eating is not possible

MDI = multiple daily insulin injection; CSII = continuous subcutaneous insulin injection.

For women with preexisting diabetes, maintaining close-to-normal blood glucose levels is essential for avoiding maternal and fetal complications.

Both premeal and postprandial (6–8 times a day) and bedtime blood glucose monitoring is recommended, especially for women receiving multiple daily insulin injections (MDIs) or continuous subcutaneous insulin infusion (CSII) therapy. Middle-of-the-night monitoring is recommended if there is a suspicion of nighttime hypoglycemia. Precise monitoring schedules should be individualized.

Fingerstick SMBG is best during pregnancy, since alternate site testing may not identify rapid changes in glucose concentrations characteristic of women with diabetes.

Recording food intake along with SMBG results 2 to 3 days before a follow-up visit is helpful. It provides data to determine whether the cause of any hyperglycemia is inadequate insulin dosing or excessive carbohydrate intake. Such a record also allows for calorie or nutrient calculations.

Because even mild A1C elevations are associated with increased fetal morbidity, A1C testing should be performed at the initial visit during pregnancy, monthly until target levels <6.0 are achieved, and then every 2 to 3 months thereafter.

Urine ketone monitoring is recommended during illness, when blood glucose levels exceed 200 mg/dL, or when the woman is unable to eat due to nausea or vomiting. Ketones cross the placenta and may be harmful to the fetus.

## General Guidelines for All Pregnant Women

- Take vitamin–mineral supplement (smokers, women with inadequate dietary intake)
- Follow daily reference intakes: calcium, 1000 mg/d; folic acid, 600 µg/d
- Avoid alcohol and smoking
- Limit caffeine to <300 mg/d, artificial sweeteners to 3–4 portions/d
- Consume fish rich in omega-3 fatty acids, but avoid fish potentially high in mercury
- Monitor weight gain at each office visit

Pregnant women with diabetes should follow general guidelines for all pregnant women, in addition to guidelines developed specifically for women with diabetes.

A woman who has inadequate dietary intake or is a cigarette smoker may need a daily vitamin–mineral supplement.

Women should follow the dietary reference intakes (DRIs) for pregnancy established by the Institute of Medicine (IOM). DRIs are 1000 mg/d for calcium (1 cup of milk has about 300 mg of calcium) and 600 µg/d for folic acid. Folate supplementation during pregnancy is associated with a decreased incidence of small-for-date births and neural tube defects.

Pregnant women should be counseled to avoid alcohol and smoking. They should limit their caffeine intake to <300 mg/d (about 2 cups of coffee).

Consumption of artificial sweeteners approved by the US Food and Drug Administration is considered safe during pregnancy as long as the Acceptable Daily Intake is not exceeded. The recommended limit is 3 to 4 portions per day.

Pregnant women should eat at least 2 meals of oily ocean fish per week to increase omega-3 fatty acids, but should avoid eating fish potentially high in methylmercury (eg, swordfish, king mackerel). State health departments can provide useful guidance.

Weight should be monitored at each visit to ensure that weight gain goals are met. For a normal-weight woman, gains of <2 lb or >6.5 lb per month may require further evaluation.

## MNT: General Energy and Nutrition Recommendations

- Refer to dietitian for individualized meal plan
- Calories
  - No change in 1st trimester
  - About 300 additional kcal/d in 2nd and 3rd trimesters
- Weight gain recommendations based on prepregnancy body mass index (BMI)
  - Normal BMI (19.6–26 kg/m<sup>2</sup>)                      25–35 lb
  - Underweight (<19.6 kg/m<sup>2</sup>)                      35–45 lb
  - Overweight (>26–29 kg/m<sup>2</sup>)                      15–25 lb
  - Obese (≥30 kg/m<sup>2</sup>)                                      15 lb
- Protein consumption: 1.1 g · kg<sup>-1</sup> · d<sup>-1</sup>
- Digestible carbohydrate consumption: 175 g/d

The ADA recommends that women with diabetes receive individualized MNT as needed to achieve treatment goals, preferably by a registered dietitian familiar with the components of MNT for diabetes and pregnancy.

Unless a woman is underweight, energy intake does not need to increase during the first trimester. Energy requirements increase during the second and third trimesters, and dietitians usually recommend adding about 300 kcal/d to a woman's prepregnancy energy needs during that period.

Weight-gain goals are based on the woman's prepregnancy body mass index (BMI), and are as follows:

<u>BMI (kg/m<sup>2</sup>)</u>	<u>Weight Gain (lb)</u>
19.6–26 (normal)	25–35
<19.6 (underweight)	35–45
>26–29 (overweight)	15–25
≥30 (obese)	15

Protein requirements increase during the second and third trimesters to support expansion of the blood volume, uterus, and breasts, and synthesis of fetal and placental proteins. The recommended level of protein consumption is 1.1 g · kg<sup>-1</sup> · d<sup>-1</sup>.

The DRI/Recommended Daily Allowance for carbohydrate is 175 g/d. This is about 45 grams above the nonpregnant carbohydrate intake. Low carbohydrate diets are not recommended during pregnancy.

## MNT Basics for Women with Preexisting Diabetes

- Balance food intake with insulin administration to maintain glucose control
- Make necessary modifications during first trimester
  - Increased risk for hypoglycemia: may need less insulin or more snacks
  - Morning sickness: adjust insulin or food intake
- Follow basic nutrition guidelines
  - 2–3 fruit servings
  - 3–5 vegetable servings
  - 2–3 calcium-rich food servings
  - 2 protein servings

Pregnant women with preexisting diabetes need to balance food intake with insulin to maintain euglycemia. Women should be counseled about insulin-to-carbohydrate ratios so appropriate insulin doses can be given to balance the carbohydrate content of meals and snacks.

During the first trimester, hormonal changes may result in erratic blood glucose levels. The increased risk for hypoglycemia during this time may necessitate adjustments in insulin or in food intake. Frequent, smaller meals and snacks may be helpful. The nausea and vomiting of morning sickness may also require adjustments in diet and insulin.

In general, nutritional guidelines for pregnant women with type 1 or type 2 diabetes are similar to recommendations for pregnant women who do not have diabetes. The daily diet should include 2 to 3 servings of fruit, 3 to 5 servings of vegetables, 2 to 3 servings of calcium-rich foods, and 2 servings of protein. Healthcare providers should promote consumption of a wholesome, balanced diet consistent with ethnic, cultural, and financial considerations.

## Guidelines for Physical Activity During Pregnancy

- Obtain physician clearance
- Understand benefits of main categories: aerobic, resistance, flexibility
- Identify appropriate types of exercise
  - Individualized program with realistic goals
  - Certain exercises contraindicated during pregnancy (eg, supine after 1st trimester)
- Monitor maternal and fetal well-being during activity
- Use strategies for preventing and treating hypoglycemia

Physician clearance is recommended before a pregnant woman with preexisting diabetes or GDM embarks on an exercise program. In the absence of contraindications, women can maintain a moderate activity level.

Exercise can be broadly divided into aerobic (cardiovascular), resistance (strength), and flexibility (stretching) activities.

Women should consult a professional to identify appropriate types of exercise and develop an individualized program with realistic goals. Programs should reflect the physical activity level of the woman before she became pregnant, her current fitness level, and weeks of gestation. Low-impact activities such as walking, swimming, or using a stationary bike are preferable to strenuous activities and contact sports. Certain exercises, such as those performed in a supine position after the first trimester, are not appropriate because they may place stress on the fetus. As a rule, women should limit their physical activity to 15 to 30 minutes.

Women should learn to monitor their well-being (especially their heart rate) during physical activity. They can also be taught to monitor their breathing (using a talk test), temperature, and muscle fatigue. They should also monitor fetal activity before and after exercise.

Because exercise can lead to hypoglycemia, the patient should be instructed to test blood glucose levels before and after exercise and to consume 15 to 30 grams of carbohydrate if blood glucose is low.

## Insulin Therapy for Women with Preexisting Diabetes

- Meeting basal and prandial insulin needs with intensified insulin regimens usually results in optimal control
- Prandial insulin doses should be matched to carbohydrate intake, premeal blood glucose, anticipated activity level
- Type 1 diabetes: using algorithm to adjust premeal insulin doses to correct for glucose values outside target range is usually appropriate
- Type 2 diabetes
  - Women receiving oral antidiabetic medications should switch to insulin
  - Initial total daily insulin dose of 0.7–1.0 units/kg body weight is often effective

For optimal glycemic control in pregnant women with preexisting diabetes, provision of basal and prandial insulin needs with intensified insulin regimens (multiple dose regimens of subcutaneous long- and short-acting insulins or CSII) usually gives the best results. The multiple adjustable basal rates offered by CSII can be especially useful for patients with daytime or nocturnal hypoglycemia or a prominent dawn phenomenon (increased insulin requirement between 4 AM and 8 AM).

A study comparing the use of CSII therapy with MDIs in women with type 1 diabetes found that achieving good metabolic control was the critical factor in avoiding risk of fetal malformation, regardless of whether control was achieved by CSII therapy or the use of MDIs. A study in women with type 2 diabetes showed that use of a pump was well tolerated, especially in those taking large amounts of insulin; however, use of a pump was associated with weight gain.

Prandial insulin doses should be matched to carbohydrate intake, premeal blood glucose, and the anticipated level of activity.

In women with type 1 diabetes, there may be a period of increased insulin sensitivity at 10 to 14 weeks' gestation. Thereafter, the required insulin dose usually rises sequentially, with wide individual variations, often leveling off or declining after 35 weeks. An algorithm for adjusting premeal insulin doses to correct for glucose values outside the target range is appropriate for most patients.

Women with type 2 diabetes who are receiving oral antidiabetic medications should switch to insulin. For this conversion, an initial daily dose of 0.7 to 1.0 units/kg actual body weight is often effective, with subsequent adjustments for blood glucose concentrations. Women with obesity may require a higher insulin dosage than nonobese women. During the course of pregnancy, insulin requirements may double or triple.

## Insulin Analogs in Pregnancy: Preexisting Diabetes

- Pregnancy categories
  - Rapid-acting: insulins lispro and aspart, B; insulin glulisine, C
  - Long-acting: insulins glargine and detemir, C
- Insulins lispro and aspart may produce better postprandial control with less hypoglycemia than premeal regular insulin; data for insulin glulisine not yet available
- Patients taking insulins glargine or detemir should be transitioned to neutral protamine Hagedorn (NPH) insulin 2 or 3 times daily

Clinical trials have shown that the rapid-acting insulin analogs insulin lispro and insulin aspart are safe and effective for the treatment of pregnant women with preexisting diabetes, and these analogs have a pregnancy category “B” rating. Due to the current lack of data in pregnant women, insulin glulisine has a “C” rating. Both long-acting insulin analogs have a “C” rating due to insufficient evidence in pregnancy, although studies whose results have recently been reported suggest that insulin glargine may be safe and effective during pregnancy.

Data suggest that the rapid-acting analogs insulins lispro and aspart may produce better postprandial control with less hypoglycemia compared with the use of premeal regular insulin. Pending the availability of safety and efficacy data from controlled clinical trials, patients who are taking insulin glargine or insulin detemir should be transitioned to neutral protamine Hagedorn (NPH) insulin 2 or 3 times daily, preferably before pregnancy or at the first prenatal visit.

## Achieving a Successful Pregnancy

- Goals: healthy mother and healthy term infant
- Contributors to success
  - Regular visits to team members
  - Strong self-management and knowledge skills
  - Monitoring of weight changes
  - Weekly insulin adjustments
  - Consistent food intake
  - Monitoring of maternal health
  - Monitoring of fetal development

The goals of pregnancy are to maintain the health of the mother and to produce a healthy term infant. To achieve these goals, the medical, physical, and psychological needs of the woman must be met throughout the pregnancy and the postpartum period.

Using a team approach with the woman as the center of the team increases the likelihood that these goals will be achieved.

Contributors to success are regular visits to team members throughout the pregnancy, strong self-management skills, monitoring the patient for weight changes, weekly insulin adjustments if needed, maintenance of consistent and appropriate food intake, monitoring of maternal health, and monitoring of fetal development.

## Barriers to Successful Outcomes

- Fear of physiological changes, worsening of diabetes, not producing a healthy baby
- Absence of emotional and financial support
- Lack of psychosocial assessment/ counseling
- Absence of an individualized management plan
- Lack of adequate follow-up visits and appropriate monitoring

Major barriers to successful outcomes in pregnant women with diabetes have been identified. These include fears of physiological changes, the worsening of diabetes, and of not producing a healthy baby. Other barriers are the absence of emotional support, the lack of psychosocial assessment and/or counseling, the absence of an individualized management plan, and the lack of adequate follow-up visits to team members during the postpartum period.

Although all women go through adjustment stages during their pregnancy, in women with diabetes these stages are complicated by the need to achieve better glycemic control during pregnancy. Increased anxiety about the effects of diabetes on herself and on the fetus, as well as doubts about her ability to manage both pregnancy and diabetes, may compromise a woman's willingness to undertake the added responsibility of close adherence to a demanding treatment plan.

The intensity of following an intense self-management regimen "emotionally lengthens" the time span of the pregnancy for even the most motivated patient. Therefore, emotional support, whether provided by the spouse, other family members, healthcare professionals, peers, or support groups, is an essential part of well-being. A psychosocial assessment can provide valuable information about lifestyle, family, job, and economic situation, and can determine whether additional counseling is appropriate.

Psychological disorders, which can affect glycemic control, are detectable in up to one third of patients with diabetes, including pregnant women. Therefore, these women should be screened for depression, anxiety/stress, and disordered eating, and the team management plan adjusted as indicated.

A management plan that is not individualized will fail to maximize the woman's adaptation to pregnancy in the context of diabetes.

Adequate follow-up visits during the postpartum period are essential. At that time, the woman will need to learn to balance her own self-care needs with the needs of her infant.

## Maternal Complications Associated with Poor Outcomes

- Poor maternal glucose control
  - Ketoacidosis, associated intrauterine deaths
  - Birth anomalies most common in women with poor blood glucose control during first trimester
  - Food plan and insulin regimen don't match
- Vascular disease
  - Hypertension
  - Preeclampsia/eclampsia
- Microvascular disease (especially nephropathy)

Metabolic control is an important predictor of perinatal outcome. Major congenital anomalies are most common in women with poor blood glucose control. The glucose level at which a woman will spill ketones is reduced during pregnancy. Ketones cross the placenta and may be harmful to the fetus. A fetal loss rate of 30% has been reported with maternal acidosis and coma. Some evidence suggests that elevated maternal ketones are associated with lower IQ scores in offspring.

Vascular complications, especially hypertension and preeclampsia/eclampsia, may adversely affect outcome. The greater the degree of hypertension, the greater the likelihood of a poor outcome for mother and child. Preeclampsia is defined by systolic blood pressure  $>140$  mm Hg or diastolic blood pressure  $\geq 90$  mm Hg in a woman who was normotensive before pregnancy, together with proteinuria. In the absence of proteinuria, preeclampsia may be suspected if the elevated blood pressure is accompanied by headache, blurred vision, and abdominal pain, or by abnormal liver enzymes and low platelet counts. Eclampsia is the occurrence of seizures that cannot be attributed to other causes in a woman with preeclampsia. Preeclampsia/eclampsia is a major cause of maternal and/or fetal morbidity and mortality. Associated complications include placental abruption, cerebral hemorrhage, pulmonary edema, acute renal failure, and liver infarction.

Another predictor of poor outcome is microvascular disease (especially nephropathy). Patients with nephropathy are at increased risk for preeclampsia, fetal-growth restriction, and preterm delivery, and have a 3-fold increase in the rate of stillbirth over women who have diabetes but who do not have nephropathy.

## Other Maternal Complications

- Genitourinary infections
- Polyhydramnios
- Worsening of chronic complications
  - Retinopathy
  - Neuropathy
  - Cardiac disease
- Preterm delivery
- Cesarean section

In addition to an increased risk of poor glucose control, vascular disease, and microvascular disease during pregnancy, women with diabetes are at risk for developing other complications.

Common urinary tract infections (UTIs) are bacteriuria, cystitis (bladder infection), and pyelonephritis (kidney infection). UTIs occur in 4% to 10% of pregnant women, and diabetes increases the risk for UTI by 2- to 4-fold. Diabetes also increases the risk for vaginal infections.

Polyhydramnios, an excessive volume of amniotic fluid, occurs more often in pregnancies with fetal complications, such as congenital anomalies of the central nervous system or gastrointestinal tract, than in normal pregnancies.

During pregnancy, existing retinopathy may be exacerbated by hormonal changes, hypertension, or rapid normalization of blood glucose.

Maternal complications associated with preterm delivery include preeclampsia, decreased maternal renal function, and maternal hyperglycemia. Women with diabetes are at an increased risk for cesarean section due to macrosomia, fetal distress, and failed induction.

## Possible Fetal/Neonatal Complications

- Postpartum hypoglycemia
- Hypocalcemia
- Hypomagnesemia

Among the fetal and neonatal complications commonly observed in infants of mothers with diabetes are hypoglycemia/hyperinsulinemia, hypocalcemia, and hypomagnesemia. These complications can be prevented or their severity reduced in patients who establish and maintain near-normal blood glucose levels before and during pregnancy.

Hypoglycemia in the newborn (glucose levels  $<35$  mg/dL) is the most common neonatal metabolic complication. It occurs in 10% to 25% of all infants born to mothers with diabetes.

If maternal diabetes is poorly controlled, the fetus receives more glucose and alternate fuel sources than it requires for normal growth, and must secrete additional amounts of insulin to use this excess glucose. At delivery, the glucose supply decreases but the baby continues to secrete high amounts of insulin. This can result in neonatal hypoglycemia, which is usually treated by early feeding and, if necessary, by the administration of IV glucose.

Hypocalcemia, which has an incidence of about 50%, and hypomagnesemia, which has an incidence of about 33%, are neonatal complications that should be promptly diagnosed and treated. These conditions are probably related to the severity of maternal diabetes, which can cause secondary transient hypoparathyroidism during the first 2 to 4 days of life.

Hypomagnesemia may be the result of blunted secretion of parathyroid hormone; hypocalcemia may be secondary to hypomagnesemia.

## Other Possible Fetal/Neonatal Complications

- Polycythemia
- Cardiomyopathy
- Hyperbilirubinemia
- Respiratory distress syndrome
- Stillbirth

Other possible fetal or neonatal complications associated with diabetes are polycythemia, cardiomyopathy, hyperbilirubinemia, and stillbirth and respiratory distress syndrome (RDS).

Fetal polycythemia is associated with increased levels of erythropoietin. This complication is probably secondary to chronic intrauterine hypoxia caused by hyperglycemia and hyperinsulinemia. The anabolic effect of hyperinsulinemia can also lead to cardiomyopathy.

The cause of hyperbilirubinemia is multifactorial. Potential causes include increased hemolysis and ineffective erythropoiesis, increased bruising and trauma, and a delay in liver enzyme maturation. Venous hematocrits ranging from greater than 65% to 70% have been observed in 20% to 40% of newborns during the first days of life.

In 1976, it was estimated that the relative risk of RDS in neonates of diabetic mothers whose gestational age was  $\leq 38$  weeks was more than 5 times higher than in neonates of nondiabetic mothers. Today, the rate of RDS is markedly lower, due to demonstrated evidence that glycemic control during pregnancy is critical, the greater likelihood of extending pregnancy beyond 38 weeks, and the availability of sophisticated monitoring techniques.

The incidence of stillbirth has also decreased in recent years, at least in patients who have received preconception care. However, a French study whose results were reported in 2003 found that the perinatal mortality rate in infants born to mothers with preexisting diabetes was 4.4%, compared with a rate of 0.7% in the general population. Stillbirths accounted for 79% of the perinatal deaths in this cohort. Only 40% of the mothers in the study had received preconception care.

## Fetal Macrosomia

- Birth weight >4000 g (8.8 lb) or >90th percentile for gestational age
- Most common complication of GDM; also occurs in types 1 and 2 diabetes
- Increasing incidence in United States and other developed countries
- Mainly affects heart, liver, subcutaneous fat
- Traumatic birth injuries: shoulder dystocia, fractured clavicles, brachial plexus injury, asphyxia
- Increased rate of surgical delivery
- Can lead to early-onset obesity and type 2 diabetes in the child

Macrosomia is typically defined as a neonate weighing more than 4000 grams (8.8 lb) or that is in greater than the 90th percentile for gestational age, although other definitions are also used. Macrosomia is the most common neonatal complication of GDM, with reported prevalence ranges of 15% to 45% and 10% to 30%. Macrosomia also occurs in preexisting types 1 and 2 diabetes. Its incidence is increasing in the United States and other developed countries, possibly because of rising rates of obesity and diabetes. Macrosomia mainly affects fetal heart, liver, and subcutaneous fat. Common neonatal complications are shoulder dystocia, fractured clavicles, and brachial plexus injury. Macrosomia increases the demand for oxygen. Therefore asphyxia, which is associated with difficult labor and delivery, may result. Macrosomia also increases the likelihood of surgical delivery.

Possible long-term consequences of macrosomia in the offspring of mothers with preexisting diabetes or GDM are obesity and type 2 diabetes. These effects, which may manifest during childhood, are not due to genetic factors alone. Instead, the consequences of maternal diabetes and macrosomia are increasingly seen as a vicious cycle. Children of mothers who had diabetes during pregnancy are at increased risk of becoming obese and developing diabetes at young ages. Many female offspring already have diabetes or abnormal glucose tolerance by the time they reach their childbearing years, thereby perpetuating the cycle.

## Possible Congenital Anomalies: Preexisting Diabetes

Anomaly	Ratio of Incidence*
Caudal regression	252
Situs inversus	84
Renal anomalies (total)	38
Heart anomalies	4
Anencephalus	3
Anal/rectal atresia	3
Spina bifida, other CNS	2

CNS = central nervous system.

\*Comparison to general population.

Most of the congenital anomalies observed in infants of diabetic mothers involve the central nervous system and the cardiovascular, gastrointestinal, genitourinary, and skeletal systems.

Congenital anomalies in infants of diabetic mothers are more commonly multiple, more severe, and more often fatal than those found in the general population.

An analysis comparing the incidence of congenital anomalies in the infants of mothers with diabetes compared with the general population has shown that caudal regression syndrome, situs inversus, and renal anomalies are the anomalies most strongly associated with diabetes. Caudal regression syndrome is a structural disorder characterized by abnormal development of the lower part of the fetal spine. Situs inversus is a structural anomaly in which the positions of the major visceral organs are reversed.

## Monitoring Fetal Status

Test	Purpose	Timing	Comment
Ultrasound (U/S)	Screen for structural anomalies; assess fetal growth	After 7.5 wks; comprehensive U/S at 18–22 wks and at 28–40 wks	Detects major anomalies; serial U/S to assess growth
$\alpha$ -Fetoprotein	Screen for open fetal defect	15–18 wks	Detects neural tube defects
Amniocentesis	Assess lung maturity	Late 3rd trimester	If birth will be induced before 39 weeks

In women with diabetes, tests that monitor fetal status are performed at the healthcare provider's discretion, based on individual needs.

The most commonly performed test is ultrasound monitoring. Ultrasound is used during the first trimester to estimate the date of delivery, during the second trimester to identify structural abnormalities, as indicated during the third trimester to assess fetal growth and development, and as needed to measure amniotic fluid levels. In early pregnancy, ultrasound can show the presence of malformations such as neural tube defects.

Serial ultrasounds can demonstrate growth patterns that can assist in identifying infants that are large or small for gestational age. Assessing the fetal response to maternal GDM by ultrasound measurement of fetal abdominal circumference in the second and early third trimesters can provide useful information to guide management decisions.

$\alpha$ -Fetoprotein is a maternal blood test that can identify a fetus at risk for a neural tube defect. The risk of neural tube defects is 10 to 20 times greater in women with diabetes than in the general population. The  $\alpha$ -fetoprotein test is more commonly used in women with preexisting diabetes than in those with GDM due to the greater risk for neural tube defects in infants of mothers with preexisting diabetes.

If delivery is to be induced before 39 weeks, amniocentesis is performed late in the third trimester to assess lung maturity. Amniocentesis is also used to identify chromosomal abnormalities associated with birth defects. This test, which is routinely performed late in the first trimester for women over the age of 35 years, is associated with a high rate of false-positive results.

## Monitoring Fetal Status (cont'd)

Test	Purpose	Timing	Comment
Nonstress	Screen for fetal well-being	32 wks (types 1&2) 35–40 wks (GDM)	May result in false-positives
Biophysical profile	Evaluate fetal problems	32 wks (types 1&2) 35–40 wks (GDM)	Reliable profile
Fetal activity	Screen for fetal well-being	32–40 wks	Simple, inexpensive

Tests used to monitor fetal status in women with preexisting diabetes or GDM include nonstress tests, biophysical profiles, and fetal activity tests.

A reactive nonstress test (NST) evaluates the absence or presence of fetal compromise. It is recommended that it be performed at week 32 in women with preexisting diabetes and between weeks 35 and 40 in women with GDM. A limitation is that false-positive results are common.

The biophysical profile, a combination of an NST and an ultrasound evaluation, may be conducted if NST results are inconclusive. This reliable test is usually performed at week 32 in women with preexisting diabetes. In women with GDM, it is usually performed between weeks 35 and 40, although the biophysical profile is not always performed in these patients.

Depending on individual circumstances, NSTs and biophysical profiles may be done on a biweekly, weekly, or daily basis.

Fetal activity testing is a simple, inexpensive method of monitoring fetal well-being that is usually begun at about 32 weeks of gestation. The patient can use several protocols, including kick counting, to measure and record perceived fetal movements over a given time period.

## Management of Labor and Delivery

- Continuous fetal heart rate monitoring
- Maternal bedside glucose monitoring (hourly and as needed)
- Maternal plasma glucose levels maintained between 70–100 mg/dL
- Continuous infusion of insulin and/or glucose as required

In pregnancy complicated by diabetes, appropriate management during labor and delivery increases the safety of the mother and infant.

The fetal heart rate should be continuously monitored.

Maternal blood glucose levels should be maintained between 70 and 100 mg/dL. To ensure that glucose levels remain in this range, the glucose level is measured hourly and women may receive a continuous infusion of insulin and/or glucose as required.

Numerous intrapartum insulin management regimens recommend the initiation of IV insulin therapy at blood glucose levels ranging from 90 to 140 mg/dL. A useful protocol is:

- If the plasma blood glucose value is between 100 to 150 mg/dL, then insulin is added to IV saline solution and administered at the rate of 1.0 unit/hr.
- If the plasma blood glucose value is >150 mg/dL, insulin is infused at the rate of 2.0 units/hr.
- If blood glucose remains >100 mg/dL for 2 hours after initiation of insulin, the rate is increased by 0.5 unit/hr, repeated every 2 hours if blood glucose remains elevated.
- Insulin is discontinued when blood glucose levels fall to <100 mg/dL.
- If blood glucose level falls <70 mg/dL, the infusion solution is changed to 5% dextrose.
- Women with uncontrolled diabetes may need 0.5–2.5 units/hr of insulin during active labor.

Although women with GDM usually do not require insulin during labor, this protocol can be used if blood glucose values are outside the range of 70 to 100 mg/dL.

## Postpartum Follow-up: Preexisting Diabetes

- Insulin requirements are significantly lower
- Breastfeeding is recommended
- Women with type 2 diabetes may continue with insulin therapy during lactation
- Close follow-up of diabetes control is needed to reestablish baseline insulin requirement

In women with preexisting diabetes, the maintenance of euglycemia remains a major goal during the postpartum period.

Insulin requirements generally decline significantly in the period immediately after delivery, and women may need no insulin for 24 to 48 hours. Persistently elevated blood glucose levels in the early postpartum period suggest the presence of an underlying infection.

Breastfeeding is recommended for the welfare of both the mother and the infant. Breastfeeding mothers may require less insulin because of greater calories expended when nursing. In general, insulin requirements are recalculated at 0.6 unit/kg current weight for nonlactating women and 0.4 unit/kg current weight for lactating women.

Nutrition requirements for a woman with preexisting diabetes should focus on maintaining blood glucose control and meeting the nutritional needs of lactation. The same meal plan followed during the third trimester of pregnancy is usually appropriate during lactation, but addition of a bedtime or middle-of-the-night snack may be needed.

Women with type 2 diabetes whose glucose value cannot be maintained with MNT may need to continue to take insulin while breastfeeding, because oral glucose-lowering agents cannot be used during lactation.

## Key Recommendations: Preexisting Diabetes

- Receive education from early adolescence
- Have preconception counseling and pregnancy planning
- Maintain healthy lifestyle during pregnancy
  - Nutritious diet
  - Appropriate physical activity
- Use the most effective regimen for maintaining glycemic control during pregnancy
- Have appropriate postpartum follow-up

The ADA and AADE have developed several key recommendations concerning pregnancy for women with preexisting types 1 and 2 diabetes.

All women of childbearing age who have preexisting diabetes should receive education about preconception care. Ideally, this education should begin in early adolescence. Women not planning a pregnancy within the next year should be given general information regarding the risks of pregnancy and the importance of contraception and prepregnancy planning. Those planning a pregnancy within the next year should receive more detailed preconception counseling.

During pregnancy, women should maintain a healthy lifestyle, including a nutritious diet and an appropriate level of physical activity.

The most effective treatment regimen for maintaining glycemic control and avoiding hypoglycemia should be used throughout pregnancy to maximize good outcomes.

Women should receive appropriate postpartum follow-up. Important components are maternal support and education and close monitoring of glycemic control to reestablish baseline insulin requirements.

## Prevalence and Impact of GDM

- Affects 7% of all pregnancies in the US (range, 1%–14%)
- Frequency usually reflects the frequency of type 2 diabetes in the underlying population
- Increasing prevalence in most recent studies
- Macrosomia of newborn the most common complication
- Associated with increased rate of cesarean delivery

GDM complicates 7% of all pregnancies, resulting in more than 200,000 cases annually in the United States. The estimated prevalence of GDM ranges from 1% to 14% of all pregnancies, depending on the population studied and the diagnostic tests employed.

The frequency of GDM usually reflects the frequency of type 2 diabetes in the underlying population. Most recent studies have shown an increased prevalence of GDM in all ethnic groups examined. Among the US populations surveyed, increases in non-Hispanic whites ranged from 46% to 95% and an increase of 21% was documented in Native Americans. Reasons for increasing GDM rates include older maternal age, an increasing prevalence of obesity, and a decrease in physical activity.

Macrosomia of the newborn is the most common complication of GDM, resulting in increased rates of surgical delivery.

## Pathophysiology of GDM

- Incompletely understood
- Most women with GDM have chronic  $\beta$ -cell dysfunction
- Great majority of women who develop GDM have chronic insulin resistance
- Much smaller numbers have autoimmune  $\beta$ -cell dysfunction or previously undetected monogenic diabetes
- GDM is increasingly viewed as a stage in the evolution of diabetes

Today, the pathophysiology of GDM is incompletely understood.

There is growing evidence that most women with GDM have chronic  $\beta$ -cell dysfunction.

The great majority of women who develop GDM also exhibit chronic insulin resistance. A small minority (<10%) of women with GDM show evidence of autoimmune  $\beta$ -cell dysfunction and a much smaller number are found to have previously undetected monogenic diabetes (caused by a single gene or by either of an allelic pair of genes).

GDM is increasingly viewed as a stage in the evolution of diabetes.

Ongoing studies are seeking to determine the best means of preventing or delaying the progression to type 2 diabetes in women with a history of GDM.

## Risk Factors for GDM

- Family history of diabetes
- Obesity (BMI >30 kg/m<sup>2</sup>)
- Increased age
- History of abnormal glucose metabolism
- History of poor obstetric outcome or GDM
- Membership in high-risk ethnic group
- Previous large-for-gestational-age or macrosomic infant
- History of polycystic ovary disease
- Low weight at own birth

Risk factors for GDM include:

- Strong family history of diabetes in parents and/or siblings
- Obesity (BMI >30 kg/m<sup>2</sup>)
- Increased age
- History of abnormal glucose metabolism
- History of poor obstetric outcome or previous GDM
- Membership in a high-risk ethnic group, including African American, Native American, Hispanic/Latino, Asian Pacific Islander/Southeast Asian, Asian Indian, and indigenous Australian populations
- Previous delivery of a large-for-gestational-age or macrosomic infant
- History of polycystic ovary disease
- Low weight at birth

A large population-based retrospective study in the United States showed that a woman's own birth weight was inversely related to her risk of GDM, suggesting that early life factors may be important in the etiology of this disorder.

# Diabetes Care for Women with Previous or Current GDM

Preconception	Pregnancy	Labor and Delivery
If previous GDM: <ul style="list-style-type: none"> <li>• Planning/contraception</li> <li>• Potential complications</li> <li>• Preconception glucose assessment</li> </ul>	Risk assessment at first prenatal visit Screening Diagnosis: 24–28 weeks Management	Fetal monitoring Glucose/insulin monitoring Postpartum diabetes assessment and prevention

Care for the woman with a history of or current GDM includes risk-assessment, screening, and follow-up care.

Women who have had a previous pregnancy complicated by GDM require preconception planning for future pregnancies. A preconception glucose assessment is recommended for women with previous GDM.

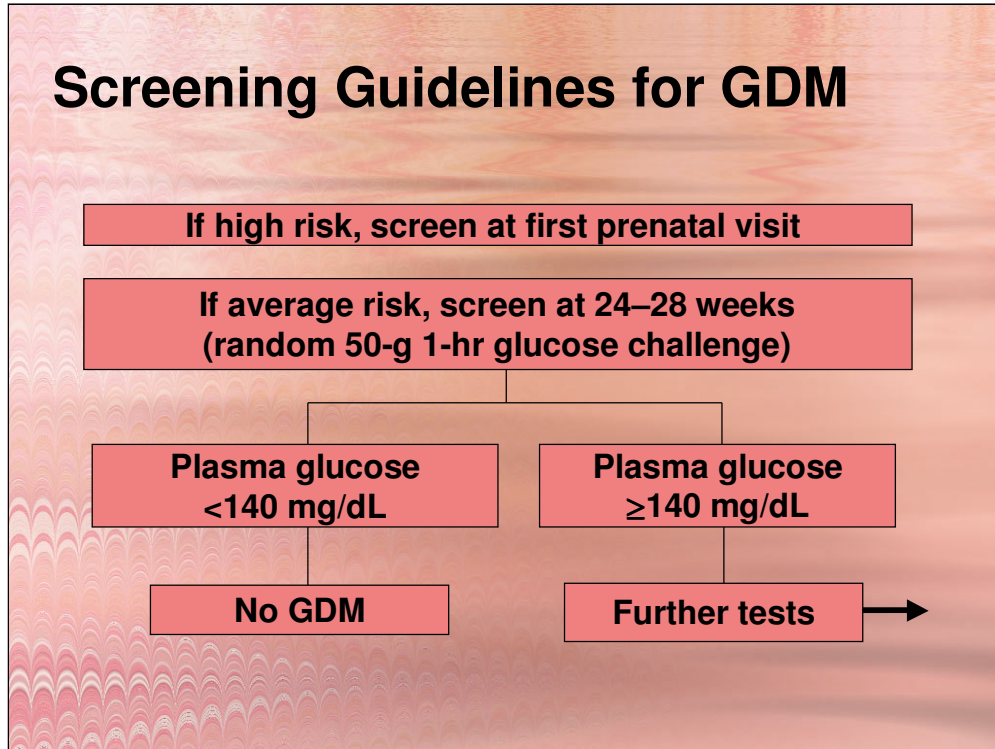
The ADA recommends that risk assessment for GDM take place at the first prenatal visit and that women at high risk for GDM undergo glucose testing.

Women at average risk for GDM and those who have not been identified as having abnormal glucose tolerance prior to week 24 of gestation should have a GDM screening test between weeks 24 and 28.

The management goal for women with GDM is to improve pregnancy outcomes by normalizing metabolism and achieving euglycemia. This is accomplished by monitoring blood glucose, MNT, administration of insulin or oral medication (if needed), and close maternal and fetal monitoring.

In the postpartum period, the woman should be retested for glucose tolerance. To reduce the risk that the patient will develop diabetes in the future, the healthcare provider should stress the importance of good nutrition and physical activity. Even if postpartum glucose tolerance is normal, women with a history of GDM should be tested annually for diabetes.

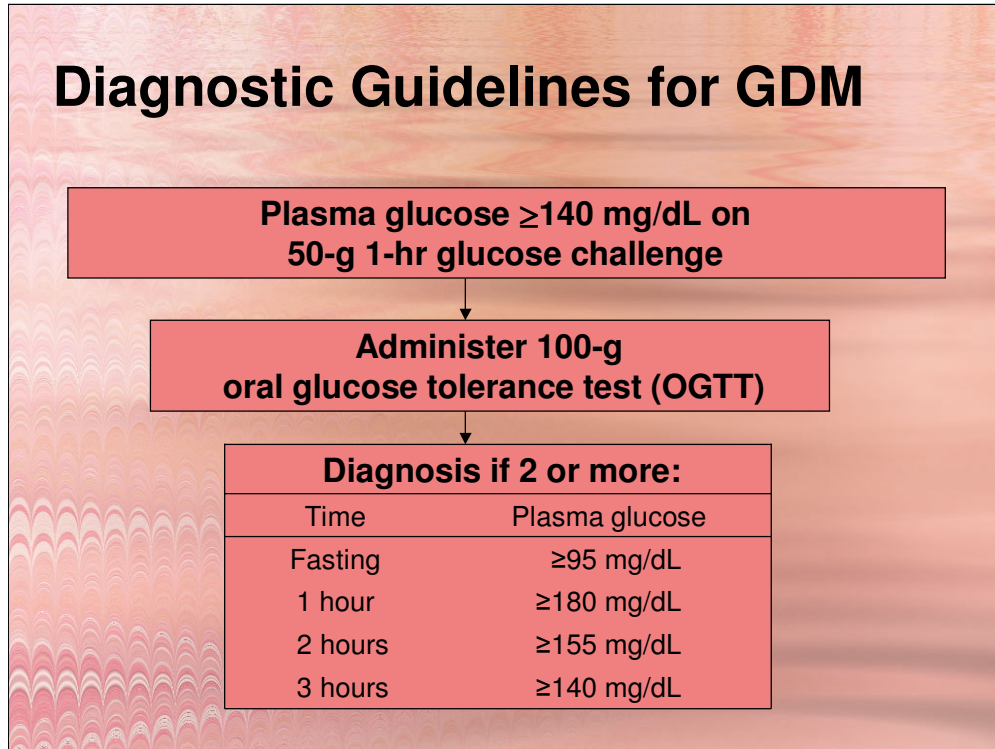
# Screening Guidelines for GDM



According to the ADA:

- Risk assessment should be conducted at the first prenatal visit to evaluate patients at high risk for developing GDM. Women at high risk should have their glucose level measured.
- Women at average risk for GDM and those who have not been identified as having abnormal glucose tolerance prior to the 24th week of gestation should have a screening test at 24 to 28 week's gestation.
- A random 50-gram 1-hr oral glucose challenge can be administered without regard for the time of day or the interval since the last meal.
- If the plasma glucose is <140 mg/dL, GDM is not present; however, high-risk individuals may be checked again later in the pregnancy.
- If the plasma glucose is ≥140 mg/dL, further testing is required.
- Although women at low risk for GDM are not routinely screened, they may be screened on the basis of clinician assessment. Low-risk women must meet the following criteria: age <25 years; no history of poor obstetrical outcome; no first-degree family history of diabetes; normal weight or underweight prior to pregnancy; membership in a low-risk ethnic group.

# Diagnostic Guidelines for GDM



If the 50-gram 1-hr oral glucose challenge screening value is  $\geq 140$  mg/dL, the next step is to administer a diagnostic oral glucose tolerance test (OGTT). This 2-step approach identifies ~80% of women with GDM.

The OGTT is performed in the morning, after an overnight fast of between 8 and 14 hours. A 100-gram glucose load is given in a volume of at least 400 mL of fluid. The test should be preceded by at least 3 days of unrestricted activity and diet. Plasma glucose levels are measured fasting and at 1, 2, and 3 hours. Definitive diagnosis requires that 2 or more of the threshold values be met or exceeded:

- A fasting plasma glucose greater than or equal to 95 mg/dL.
- A 1-hour plasma glucose greater than or equal to 180 mg/dL.
- A 2-hour plasma glucose greater than or equal to 155 mg/dL.
- A 3-hour plasma glucose greater than or equal to 140 mg/dL.

Note: A glucose load on an empty stomach can be nauseating. Counsel patients to bring a protein-rich snack to eat after testing is completed.

## Check Point

### **The correct statement about GDM is:**

- a) Overall, GDM complicates about 14% of pregnancies.
- b) Most women who develop GDM have autoimmune  $\beta$ -cell dysfunction.
- c) Women at average risk for GDM should be screened between weeks 24 and 28.
- d) The prevalence of GDM is similar in all ethnic groups.

The correct statement about GDM is:

- a) Overall, GDM complicates about 14% of pregnancies.
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The answer is c.

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## Medical Nutrition Therapy: GDM

- MNT is the cornerstone of treatment for GDM
- Food plan should fulfill minimum Institute of Medicine nutrient requirements for pregnancy
- Plan should be culturally appropriate and individualized
- Basis of MNT for GDM is a carbohydrate-controlled food/meal plan
  - Eat 3 small to moderate meals with 2–4 snacks
  - Avoid high-carbohydrate foods such as regular soft drinks

MNT is the primary treatment for GDM. A woman with GDM should receive nutritional counseling by a registered dietitian when possible or by a qualified individual with experience in GDM management. A referral to a dietitian should be made within 48 hours of the GDM diagnosis, and the initial visit should take place within 1 week of the referral.

The food plan should fulfill minimum nutrient requirements for pregnancy set by the IOM and achieve glycemic goals without inducing weight loss and ketonemia. The plan should be culturally appropriate and individualized to take into account the patient's general condition, weight gain, and physical activity. It should be modified as needed throughout pregnancy to achieve treatment goals. Nutrition interventions should emphasize overall healthy food choices, portion control, and cooking practices that can be continued postpartum and that may help prevent later type 2 diabetes and obesity.

The basis of MNT for GDM involves a carbohydrate-controlled food/meal plan. Carbohydrate should be distributed into 3 meals and 2 to 4 snacks. Consumption of foods high in total carbohydrate or sucrose, such as regular soft drinks, is not recommended.

## Meal Planning in GDM

- Follow carbohydrate consumption guidelines
  - Breakfast: 15–45 g
  - Lunch and dinner: 45–75 g each
  - Snacks: 15–45 g
- Avoid breakfast cereals and other highly processed carbohydrates
- Incorporate nutrient-rich carbohydrates in the diet
- Shift milk and fruit from mealtime to snacktime
- Eat 1–2 oz of protein with breakfast or snacks

Although meal plans should be individualized for women with GDM, some general meal planning practices are widely applicable.

Starting food plans often suggest the following carbohydrate ranges for each meal and snack:

- Breakfast: 15 to 45 g
- Lunch and dinner: 45 to 75 g each
- Snacks: 15 to 45 g each

Due to elevated hormone levels in the morning, the postbreakfast glucose level is typically the most difficult value to achieve. Therefore, carbohydrate intake should be limited to 15 to 45 grams at breakfast. Breakfast cereals are often discouraged because they generally contain more than 45 g of carbohydrate. Furthermore, breakfast cereals and other highly processed foods are more likely to raise postmeal glucose levels than less-processed, high-fiber foods.

In their eagerness to control their carbohydrate consumption, women may cut back on nutrient-rich carbohydrates such as fruit, milk, and starches. Milk and fruit are often shifted from mealtime to snacktime so that the woman can eat a larger portion of starch during meals.

The addition of 1 to 2 ounces of protein to breakfast or a snack is a good way to add calories without compromising glucose levels.

## Monitoring in Women with GDM

- SMBG
  - Once in morning (fasting)
  - 1 to 2 hours after each meal
- Monitor for urine or blood ketones if food intake is insufficient
- A1C monitoring usually limited to women diagnosed in first trimester

The ADA and the American College of Obstetrics and Gynecology support the use of SMBG in women with GDM. Women should monitor blood glucose at least 4 times daily: once in the morning (fasting) and 1 to 2 hours after each meal.

Women with insufficient food intake should monitor their urine or blood ketones. They may have insufficient food intake due to not following the appropriate food/meal plan, nausea, vomiting, or intentionally undereating to control blood glucose levels. Eating too little or eating at prolonged intervals may cause a shift from carbohydrate to fat metabolism, resulting in rises in plasma and urinary ketones.

The role of A1C testing in women with GDM has not been established; however, A1C monitoring may be used in women diagnosed with GDM during the first trimester.

## Oral Agents for GDM

- ❑ In a randomized controlled trial, glyburide and insulin had similar effects on glycemic control and neonatal outcomes
- ❑ Glyburide is a useful adjunct to MNT/physical activity regimens when additional therapy is needed to maintain target glucose levels
- ❑ The Metformin in Gestational Diabetes trial has shown that metformin is not associated with more perinatal complications than insulin
- ❑ Preliminary data suggest that acarbose may hold promise for the treatment of GDM
- ❑ Thiazolidinediones should not be used until more data are available

In general, oral antidiabetic agents have not been recommended during pregnancy because of possible teratogenic effects and neonatal hypoglycemia. Unlike first-generation sulfonylureas, which cross the placenta and stimulate neonatal insulin secretion, second-generation agents such as glyburide do not significantly cross the placenta. A randomized controlled trial reported in 2000 compared the use of insulin and glyburide in women with GDM. In this study, treatment with either agent resulted in comparable glycemic control and similar neonatal outcomes. No detectable glyburide levels were found in umbilical cord blood, and the investigators concluded that glyburide can be safely used in GDM. Subsequent retrospective studies suggested that glyburide results in lower mean glucose values, better glycemic control, and fewer hypoglycemic episodes than insulin. Larger randomized trials are now needed.

The oral biguanide metformin crosses the placenta, but the Metformin in Gestational Diabetes (MiG) trial has shown that treatment with metformin (alone or with supplemental insulin) is not associated with increased perinatal complications.

Acarbose, an  $\alpha$ -glucosidase inhibitor, is not systemically absorbed to an appreciable extent. In a randomized trial that compared acarbose and insulin in GDM, glucose control was similar with the two treatments, although gastrointestinal adverse events were common with acarbose. Acarbose may be useful for the treatment of GDM if the limitation of gastrointestinal disturbance can be overcome.

The thiazolidinediones, including rosiglitazone and pioglitazone, are agonists for the peroxisome proliferator-activated receptor- $\gamma$ . Because these agents are associated with serious hepatic and cardiovascular adverse events, and data on their use in pregnant women have not been reported, they should not be used for the treatment of GDM until more data are available.

## Insulin Therapy for GDM

- Insulin recommended when fasting plasma glucose (FPG) exceeds 105 mg/dL or postprandial glucose is elevated
- If only postprandial glucose levels are abnormal, mealtime insulin may suffice
- If FPG is also elevated, intermediate- or long-acting insulin may also be required
- Twice-daily or intensive therapy may be needed
- In clinical trials, the rapid-acting insulin analogs insulin lispro and insulin aspart were safe and effective in women with GDM

In women with GDM, initiation of insulin therapy is recommended when MNT fails to maintain fasting plasma glucose (FPG) at levels  $\leq 105$  mg/dL. Based on an extensive review of insulin management approaches described in the medical literature, Langer has estimated that 10% to 70% of women with GDM will need insulin therapy in addition to MNT. If only postprandial glucose levels are abnormal, rapid-acting insulin may suffice. If FPG is also elevated, intermediate- or long-acting insulin may also be required. Some patients may require twice-daily or intensive therapy to maintain good glycemic control.

The insulin analogs are not approved for use in pregnancy, but some studies have explored their use in pregnant women. If postprandial glucose is the target of treatment, the rapid-acting analogs insulin lispro and insulin aspart appear to be as safe and effective as regular human insulin in women with GDM and achieve better postprandial glucose concentrations with less late prandial hypoglycemia. If the patient has elevated fasting and postprandial blood glucose levels and requires MDIs, a basal-bolus regimen should be considered. Although the long-acting insulin analogs do not have as pronounced a peak effect as NPH insulin and therefore cause less nocturnal hypoglycemia, the safety of these analogs must be further established in pregnant women.

## Check Point

### **A difference between the management of pregnant women with preexisting diabetes and GDM is:**

- a) Nonstress testing and the biophysical profile are often performed later in women with GDM.
- b) Most women with GDM do not need to monitor their ketone levels.
- c) Glyburide therapy should be reserved for women with preexisting diabetes.
- d) Exercise is contraindicated in women with preexisting diabetes after the first trimester.

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The answer is a.

Nonstress testing and the biophysical profile are often performed later in women with GDM.

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Nonstress testing and the biophysical profile are often performed later in women with GDM.

## Future Risks: Women with History of GDM

- 30%–84% risk of GDM in subsequent pregnancies
- 40%–60% risk of developing type 2 diabetes within 5–15 years
- Rate of developing type 2 diabetes in women with impaired glucose tolerance: 17.1%/yr with GDM; 9.8%/yr without GDM
- Independent predictors of type 2 diabetes after GDM: elevated FPG, high BMI before or during pregnancy

Women with a history of GDM have a 30% to 84% risk of recurrent GDM in subsequent pregnancies. Lower rates are found in non-Hispanic white populations and higher rates are found in minority populations.

The risk of developing type 2 diabetes in the 5 to 15 years following GDM ranges from 40% to 60%, compared with a 15% risk in the general population.

In the Diabetes Prevention Program trial, which enrolled patients with impaired glucose tolerance, the rate of developing type 2 diabetes was 17.1% per year in women with a history of GDM and 9.8% per year in women without a history of GDM.

Independent predictors of developing type 2 diabetes after GDM are elevated FPG and high maternal BMI before or during pregnancy.

## Postpartum Follow-up: GDM

- A few fingerstick glucose tests in first days after delivery
- 75 gram 2-hr OGTT at 6–12 weeks (or later) after delivery; annual FPG test if results normal
- Plan for appropriate contraception
- Modification of risk factors for future diabetes and cardiovascular disorders
- Preconception counseling before next pregnancy
- Monitoring of child's growth and development

In the days immediately after delivery, glucose control returns to normal in more than 90% of women. However, it is important to rule out persistent diabetes by a few fingerstick glucose tests. FPG values <126 mg/dL and casual plasma glucose values <200 mg/dL rule out diabetes.

Women without immediate evidence of diabetes should have a 75-gram, 2-hour OGTT 6 to 12 weeks after delivery. This identifies women as having impaired glucose tolerance (IGT) or diabetes. IGT is defined as a plasma glucose value of 140 to 199 mg/dL; diabetes is a value of  $\geq 200$  mg/dL. Among women who were diagnosed with GDM and received treatment during gestation, follow-up testing identified a prevalence of IGT ranging from 7% to 29% and a prevalence of diabetes ranging from 5% to 14%. Women with normal test results should have a follow-up OGTT every year. A method of contraception should be chosen that does not increase the risk for glucose intolerance.

Because the Diabetes Prevention Program and other randomized controlled trials have shown that several interventions can significantly delay or prevent the development of type 2 diabetes in women with IGT, the clinician should help the patient develop and follow a treatment plan that incorporates an appropriate diet, planned exercise for 30–60 minutes per day on at least 5 days, and antidiabetic medications (if warranted). These women should also be assessed for cardiovascular risk factors, with appropriate management and follow-up, to reduce the risk of coronary heart disease, cardiomyopathy, and stroke. Diabetes screening and preconception counseling should take place before the next pregnancy is considered.

Children of mothers with GDM have an increased risk for obesity and type 2 diabetes, and their growth and development should therefore be monitored. They should be encouraged to eat a healthy diet, be active, and not become overweight.

## Major Recommendations: GDM

- Conduct risk assessment at first prenatal visit; screen high-risk women promptly
- Screen all women at 24–28 weeks' gestation
- Maintain glycemic control through MNT and exercise, adding insulin or glyburide if necessary
- Monitor woman and fetus for complications related to GDM (especially macrosomia)
- Reevaluate maternal glucose tolerance after delivery and provide ongoing monitoring and management for mother and child

Major recommendations for the diagnosis and management of GDM include the following:

At the first prenatal visit, every pregnant woman should be assessed for her risk of GDM. High-risk women should be screened as early as possible for abnormal glucose tolerance.

Women at average risk and high-risk women not previously identified as having abnormal glucose tolerance should be screened for GDM at 24 to 28 weeks' gestation.

Women diagnosed with GDM should maintain glycemic control through MNT and exercise. Insulin or glyburide should be added if needed.

The mother and fetus should be monitored for complications related to GDM, especially macrosomia.

Women should be evaluated for glucose intolerance in the immediate postpartum period and at 6 to 12 weeks after delivery. Children should be monitored for the development of obesity and type 2 diabetes on an ongoing basis and should be encouraged to follow a healthy lifestyle.

## Summary

- Diabetes increases the risk of most common complications of pregnancy and congenital anomalies.
- Advances in screening, diagnosis, and care have lowered infant mortality substantially.
- Attentive care and glycemic control before, during, and after pregnancy can reduce major complications.
- The most effective therapy for controlling fasting and postprandial blood glucose should be identified and used.

Diabetes increases the risk of the most common complications of pregnancy, as well as the risk for congenital anomalies.

Advances in screening, diagnosis, and care have lowered infant mortality rates substantially.

Attentive care before, during, and after pregnancy can reduce major complications of diabetes for mother and fetus.

The most effective therapy for controlling fasting and postprandial blood glucose should be identified and used.

Long-term monitoring and management of the mother and her child are warranted.