



American Diabetes Association

## 12. Management of Diabetes in Pregnancy

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For guidelines related to the diagnosis of gestational diabetes mellitus (GDM), please refer to Section 2. Classification and Diagnosis of Diabetes.

### Recommendations

- Provide preconception counseling that addresses the importance of tight control in reducing the risk of congenital anomalies with an emphasis on achieving A1C <7%, if this can be achieved without hypoglycemia. **B**
- Potentially teratogenic medications (ACE inhibitors, statins, etc.) should be avoided in sexually active women of childbearing age who are not using reliable contraception. **B**
- GDM should be managed first with diet and exercise, and medications should be added if needed. **A**
- Women with pregestational diabetes should have a baseline ophthalmology exam in the first trimester and then be monitored every trimester as indicated by degree of retinopathy. **B**
- Due to alterations in red blood cell turnover that lower the normal A1C level in pregnancy, the A1C target in pregnancy is <6% if this can be achieved without significant hypoglycemia. **B**
- Medications widely used in pregnancy include insulin, metformin, and glyburide; most oral agents cross the placenta or lack long-term safety data. **B**

### DIABETES IN PREGNANCY

The prevalence of diabetes in pregnancy has been increasing in the U.S. The majority is GDM with the remainder divided between pregestational type 1 diabetes and type 2 diabetes. Both pregestational type 1 diabetes and type 2 diabetes confer significantly greater risk than GDM, with differences according to type as outlined below.

### PRECONCEPTION COUNSELING

All women of childbearing age with diabetes should be counseled about the importance of strict glycemic control prior to conception. Observational studies show an increased risk of diabetic embryopathy, especially anencephaly, microcephaly, and congenital heart disease, that increases directly with elevations in A1C. Spontaneous abortion is also increased in the setting of uncontrolled diabetes. While observational studies are confounded by the relationship between elevated periconceptional A1C and other poor self-care behaviors, the quantity and consistency of data are convincing, and the recommendation remains to aim for an A1C <7% prior to conception to minimize risk (1,2). There are opportunities to educate adolescents of reproductive age with diabetes about the risks of unplanned pregnancies and the opportunities for healthy maternal and fetal outcomes with pregnancy planning (3).

Targeted preconception counseling visits should include routine rubella, rapid plasma reagin, hepatitis B virus, and HIV testing as well as Pap smear, cervical cultures, blood typing, and prescription of prenatal vitamins (with at least 400  $\mu$ g of folic acid). Diabetes-specific management should include A1C, thyroid-stimulating hormone, creatinine, and urine albumin-to-creatinine ratio testing; review of the medication list for potentially teratogenic drugs (i.e., ACE inhibitors, statins); and referral for an ophthalmologic exam.

Specific risks of uncontrolled diabetes include fetal anomalies, preeclampsia, macrosomia, intrauterine fetal demise, neonatal hypoglycemia, and neonatal hyperbilirubinemia, among others. In addition, diabetes in pregnancy increases the risk of obesity and type 2 diabetes in offspring later in life (4,5).

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## GLYCEMIC TARGETS IN PREGNANCY

The goals for glycemic control for GDM are based on recommendations from the Fifth International Workshop-Conference on Gestational Diabetes Mellitus (6) and have the following targets for maternal capillary glucose concentrations:

- Preprandial  $\leq 95$  mg/dL (5.3 mmol/L) and either
- One-hour postmeal  $\leq 140$  mg/dL (7.8 mmol/L) or
- Two-hour postmeal  $\leq 120$  mg/dL (6.7 mmol/L)

For women with preexisting type 1 diabetes or type 2 diabetes who become pregnant, the following are recommended as optimal glycemic goals if they can be achieved without excessive hypoglycemia (7):

- Premeal, bedtime, and overnight glucose 60–99 mg/dL (3.3–5.4 mmol/L)
- Peak postprandial glucose 100–129 mg/dL (5.4–7.1 mmol/L)
- A1C  $< 6.0\%$

Metabolic physiology of pregnancy is characterized by fasting hypoglycemia due to insulin-independent glucose uptake by the placenta, postprandial hyperglycemia, and carbohydrate intolerance as a result of diabetogenic placental hormones. In addition, insulin resistance increases exponentially during the second trimester and levels off toward the end of the third trimester.

Reflecting this physiology, pre- and postprandial monitoring of blood glucose is recommended to achieve metabolic control. The American College of Obstetricians and Gynecologists (ACOG) recommends the following targets: fasting  $< 90$  mg/dL, preprandial  $< 105$  mg/dL, 1-h postprandial  $< 130$ – $140$  mg/dL, and 2-h postprandial  $< 120$  mg/dL. If women cannot achieve these targets without significant hypoglycemia, the American Diabetes Association (ADA) suggests consideration of slightly higher targets: fasting  $< 105$  mg/dL, 1-h postprandial  $< 155$  mg/dL, and 2-h postprandial  $< 130$  mg/dL. Until harmonization of these guidelines is achieved, the ADA recommends setting targets based on clinical experience, individualizing care, as needed.

Due to increases in red blood cell turnover associated with pregnancy, A1C levels fall during pregnancy. Additionally, as A1C represents an average, it may not fully capture physiologically relevant glycemic parameters in pregnancy. A1C should be used as a secondary measure, next to self-monitoring of blood glucose. The recommended A1C target in pregnancy is  $< 6\%$  if this can be achieved without hypoglycemia. Given the alteration in red blood cell kinetics during pregnancy, A1C levels may need to be monitored more frequently than usual (e.g., monthly).

## PREGNANCY AND ANTIHYPERTENSIVE DRUGS

In a pregnancy complicated by diabetes and chronic hypertension, target blood pressure goals of systolic blood pressure 110–129 mmHg and diastolic blood pressure 65–79 mmHg are reasonable, as they contribute to improved long-term maternal health. Lower blood pressure levels may be associated with impaired fetal growth. During pregnancy, treatment with ACE inhibitors and angiotensin receptor blockers is contraindicated because they may cause fetal damage. Antihypertensive drugs known to be effective and safe in pregnancy include methyldopa, labetalol, diltiazem, clonidine, and prazosin. Chronic diuretic use during pregnancy has been associated with restricted maternal plasma volume, which may reduce uteroplacental perfusion (8).

## MANAGEMENT OF GESTATIONAL DIABETES MELLITUS

As highlighted in Section 2. Classification and Diagnosis of Diabetes, GDM is characterized by increased risk of macrosomia and birth complications, without a risk threshold (9). Treatment starts with medical nutrition therapy, exercise, and glucose monitoring aiming for the targets described previously. A total of 70 to 85% of women diagnosed with GDM under older criteria can control GDM with lifestyle modification alone; it is anticipated that this number will increase using the lower International Association of the Diabetes and Pregnancy Study Groups (IADPSG) thresholds. Treatment has been demonstrated to improve perinatal outcomes in randomized studies and in a U.S. Preventive Services Task Force review (10). Historically, insulin has been

the recommended treatment for GDM in the U.S. Randomized controlled trials support the efficacy and short-term safety of glyburide (11) (pregnancy category B) and metformin (12,13) (pregnancy category B) for the treatment of GDM. However, both agents cross the placenta, and long-term safety data are not available (14). Insulin also may be used and should follow the guidelines below.

## MANAGEMENT OF PREGESTATIONAL TYPE 1 DIABETES AND TYPE 2 DIABETES IN PREGNANCY

### Insulin Use in Pregnancy

Insulin is the preferred agent for management of diabetes in pregnancy because of the lack of long-term safety data for noninsulin agents. The physiology of pregnancy requires frequent titration of insulin to match changing requirements. In the first trimester, there is often a decrease in total daily dose of insulin. In the second trimester, rapidly increasing insulin resistance requires weekly or biweekly increase in insulin dose to achieve glycemic targets. In general, a small proportion of the total daily dose should be given as basal insulin and a greater proportion as prandial insulin. Due to the complexity of insulin management in pregnancy, referral to a specialized center is recommended if this resource is available. All insulins are pregnancy category B except for glargine and glulisine, which are labeled C.

### Concerns Related to Type 1 Diabetes in Pregnancy

Women with type 1 diabetes have an increased risk of hypoglycemia in the first trimester. Frequent hypoglycemia can be associated with intrauterine growth restriction. In addition, rapid implementation of tight glycemic control in the setting of retinopathy is associated with worsening of retinopathy (15). Insulin resistance drops rapidly with delivery of the placenta, and women become very insulin sensitive, requiring much less insulin than in the prepartum period.

### Concerns Related to Type 2 Diabetes in Pregnancy

Pregestational type 2 diabetes is often associated with obesity. Recommended weight gain during pregnancy for

overweight women is 15–25 lb and for obese women is 10–20 lb. Glycemic control is often easier to achieve in type 2 diabetes than in type 1 diabetes, but hypertension and other comorbidities often render pregestational type 2 diabetes as high or higher risk than pregestational type 1 diabetes (16,17).

## POSTPARTUM CARE

### Lactation

All women should be supported in attempts to nurse their babies, given immediate nutritional and immunological benefits of breastfeeding for the baby; there may also be a longer-term metabolic benefit to both mother (18) and offspring (19), though data are mixed.

### Gestational Diabetes Mellitus

Because GDM may represent preexisting undiagnosed type 2 diabetes, women with GDM should be screened for persistent diabetes or prediabetes at 6–12 weeks postpartum using nonpregnancy criteria and every 1–3 years thereafter depending on other risk factors. Women with a history of GDM have a greatly increased risk of conversion to type 2 diabetes over time and not solely within the 6–12 weeks' postpartum time frame (20). In the prospective Nurses' Health Study II (21), subsequent diabetes risk after a history of GDM was significantly lower in women who followed healthy eating patterns. Adjusting for BMI moderately, but not completely, attenuated this association. Interpregnancy or postpartum weight gain is associated with increased risk of adverse pregnancy outcomes in subsequent pregnancies (22) and earlier progression to type 2 diabetes. Both metformin and intensive lifestyle intervention prevent or delay progression to diabetes in women with a history of GDM. Of women with a history of GDM and impaired glucose tolerance, only 5–6 individuals need to be treated with either intervention to prevent one case of diabetes over 3 years (23).

### Type 1 Diabetes

Insulin sensitivity increases in the immediate postpartum period and then returns to normal over the following 1–2 weeks,

and many women will require significantly less insulin at this time than during the prepartum period. Breastfeeding may cause hypoglycemia, which may be ameliorated by consuming a snack (such as milk) prior to nursing. Diabetes self-management often suffers in the postpartum period.

### Type 2 Diabetes

If the pregnancy has motivated the adoption of a healthier diet, building on these gains to support weight loss is recommended in the postpartum period.

### Contraception

All women of childbearing age, including those who are postpartum, should have contraception options reviewed at regular intervals.

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