Gestational Diabetes

Underpinning Principles, Surveillance, and Management

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KEYWORDS

• Gestational diabetes • Glycemic intolerance • Fetal programming • Macrosomia
• Neonatal hypoglycemia • Maternal glucose control • Antenatal testing • Pregnancy

KEY POINTS

- Gestational diabetes mellitus (GDM) is defined as glycemic intolerance diagnosed at or beyond the achievement of 20 completed weeks of gestation.
- In women who ultimately develop GDM, pancreatic beta-cell compensation fails to meet the metabolic demands, creating a hyperglycemic state.
- Observational data demonstrate risks with poorly controlled GDM, including abnormal fetal growth, hypertensive disorders of pregnancy, difficult labor and vaginal delivery, increased risk of cesarean section, and the neonatal metabolic complications, including hypoglycemia, hyperbilirubinemia, and the potential for delayed pulmonary maturity.
- Poorly controlled GDM places the fetus at risk for adult-onset metabolic diseases (obesity, diabetes, hypertension, cardiovascular disease).
- Seventy percent of women with GDM will develop DM at some point in their life, and 40% to 50% of those women will develop DM within 10 years.

INTRODUCTION

The objective of this review is to provide the clinician with a working framework to evaluate and manage gestational diabetes mellitus (GDM). The American Congress of Obstetricians and Gynecologists (ACOG) defines gestational diabetes as onset of carbohydrate intolerance in pregnancy.[1] Groups such as the American Diabetes Association (ADA), World Health Organization (WHO), and International Federation of Gynecology and Obstetrics have attempted to distinguish women with likely preexisting diabetes that are first recognized in pregnancy from women whose carbohydrate intolerance is a transient condition due to pregnancy-related

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insulin resistance.[2,3] Thus, these organizations define GDM as glycemic intolerance diagnosed at or beyond the achievement of 20 completed weeks of gestation.[1–3]

Depending on the population sampled, GDM affects 3% to 25% of pregnancies.[1–4] There is an increased prevalence of GDM among African American, Pacific Islander, Hispanic, and Native American women.[2] The global prevalence of GDM has been increasing likely because of the increase of maternal obesity, delayed child bearing, and sedative lifestyles.[1–3]

Observational data demonstrate risks with poorly controlled GDM, including abnormal fetal growth, hypertensive disorders of pregnancy, difficult labor and vaginal delivery, increased risk of cesarean section, and the neonatal metabolic complications, including hypoglycemia, hyperbilirubinemia, and the potential for delayed pulmonary maturity.[1] Risks for the fetus are not limited to the gestation and subsequent neonatal period. Because of imprinting and environmental effect on gene activation, these babies are at risk for adult onset of metabolic disorders, diabetes, hypertension, obesity, cardiovascular disease, and shorter lifespan[1–4] (**Table 1**). These risks highlight the need for accurate diagnosis and proper management of GDM.[4] In the course of this review, the authors additionally discuss the emphasis on diet and activity/exercise as means of controlling blood sugars, the usual schedule of glucose monitoring, indications for medical treatment, fetal surveillance, timing of delivery, neonatal care, and postpartum care.

Physiology

In normal pregnancy, a myriad of physiologic alterations occur to promote the growth and development of the conceptus. A euglycemic state is maintained despite the fetus' energy demands via a compensatory and proliferative response within the maternal pancreas, namely the beta islet cells.[5] Conversely, in women who ultimately develop GDM, the beta-cell compensation fails to meet the metabolic demands, creating a hyperglycemic state. Data obtained from observational studies in humans and animal models have generated insights into the molecular biology leading to glycemic intolerance. Such studies demonstrate a down-regulation of insulin receptors on maternal cell surfaces in GDM.[5,6] Accordingly, these same women are biologically predisposed toward development of diabetes mellitus, type 2 later in life.[5–7] The underlying processes all lead to the assortment of metabolic derangements affecting both mother and baby that are called GDM.

Table 1
Risks associated with gestational diabetes

Maternal	Fetal
Labor dystocia	Macrosomia
Cesarean section	Hypoglycemia
Vaginal laceration	Shoulder dystocia/brachial plexus injury
Preeclampsia/gestational hypertension	Preterm delivery
Increased gestational weight gain	Delayed pulmonary maturity
DM	Metabolic syndrome in adulthood (obesity, hypertension, DM)
Cardiovascular disease	Polyhydramnios
Postpartum weight retention	Polycythemia
	Hyperbilirubinemia

Fetal Programming

Alterations of the maternal physiologic milieu inherently alter the environment for fetal development. Although lifestyle choices (smoking, diet high in fat/sugar, and sedentary lifestyle) have been widely accepted as causative in cardiovascular disease as one ages, evidence for the maternal environment having such effects on the fetus well into adulthood continues to mount.[8–11] It is now known that changes in the fetal environment alter telomere and subtelomere acetylation and methylation.[10] The flux of histone acetylation and DNA methylation impacts whether chromatin is in an open configuration and as such available for interaction with telomerase to facilitate gene transcription and/or recombination.[11] Such changes in gene activation affect predisposition toward developing chronic disease (eg, hypertension, diabetes, obesity) as the child ages.[11] In addition, there is a clear association with adulthood glucose intolerance and insulin resistance, and adaptive changes in the fetal pancreas.[12] Hence, it is imperative that clinicians provide guidance to their patients that strike the perfect balance for fetal well-being for delivery, the immediate neonatal period, and beyond.[12,13]

Last, telomere length of fetal DNA is likewise impacted by environmental insults in the maternal unit. Maternal stress and endocrine dysfunction impact fetal telomere length.[13,14] Such stressors induce telomere attrition, in turn, impacting length of the fetus' ultimate lifespan.[14] Epidemiologic data show that maternal stress leads to higher incidence of adulthood obesity, diabetes, and cardiovascular disease for their babies. As adults, these same individuals show lower cortisol, higher ACTH levels, and less prefrontal cortex and memory function when measured in stressful conditions.[14] Hence, the fetal programming phenomenon impacts the subsequent ex utero aging process and lifespan of the child well after delivery.[9]

Diagnosis

Given the lack of clear inflection point with respect to degree of gestational hyperglycemia and onset of or risk for adverse outcome, commonly cited professional organizations (eg, ACOG, ADA, WHO) vary in algorithms for diagnostic methods and interpretation of screening tests.[1–4,15] Several studies have highlighted the lack of ability to declare a clear demarcation along the continuum of hyperglycemia and outcomes.[16,17] Occult or previously undiagnosed diabetes affecting pregnancy is an issue of increasing incidence given the general trend of obesity and diabetes in the general population.[18–20] Accordingly, women identified with glycemic intolerance in the first half or before the completion of 20 weeks' gestation are diagnosed with pregestational diabetes (see Ronan Sugrue and Chloe Zera's article, "Pregestational Diabetes in Pregnancy," in this issue).[21] Women identified as having onset of glycemic intolerance in the last half of pregnancy—any time after completing 20 weeks' gestation—are classified as having GDM.[21]

Given that 90% of pregnant women in the United States present with at least one risk factor for GDM (**Fig. 1**) and 20% of those with no risk factors (**Fig. 2**) develop GDM (**Box 1**),[1,15,16,21] universal screening appears most appropriate.[1,15,16,21] Two approaches to identifying GDM exist. The most commonly used is the 2-step approach using an initial 1-hour screening 50-g glucose challenge test.[1,4,16] If negative, no further testing is required. However, screen positive individuals must undergo a formal diagnostic evaluation with a 100-g 3-hour oral glucose tolerance test (GTT). The other approach uses a singular 75-g, 2-hour GTT.[16]

Either approach is reasonable, and the choice may be made by the provider, depending on their ability to consistently implement an approach for their patient

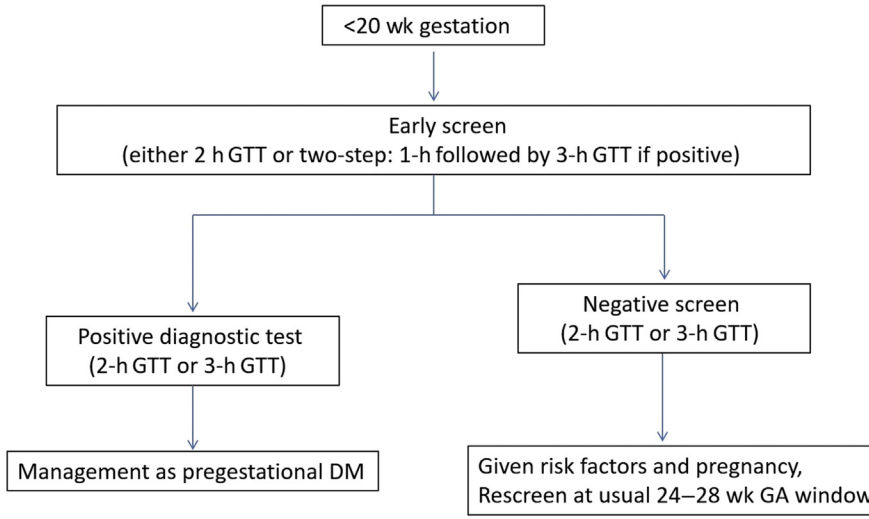

Fig. 1. Glycemic intolerance screening for patients at increased risk for insulin resistance. GA, gestational age.

population with available resources. The US Preventative Services Task Force (USPSTF) performed a systematic review on screening and deemed sufficient evidence to support universal screening but only after the achievement of 24 completed weeks' gestation.[2] Accordingly, conventional timing for screening per ACOG guidelines remains between 24 and 28 weeks, provided there is no reason to suspect underlying pregestational DM (see **Fig. 2**).[1] For those suspected to be at increased risk for underlying DM, screening should not be delayed and may be performed as early as the first prenatal visit (see **Fig. 1**).[1–4]

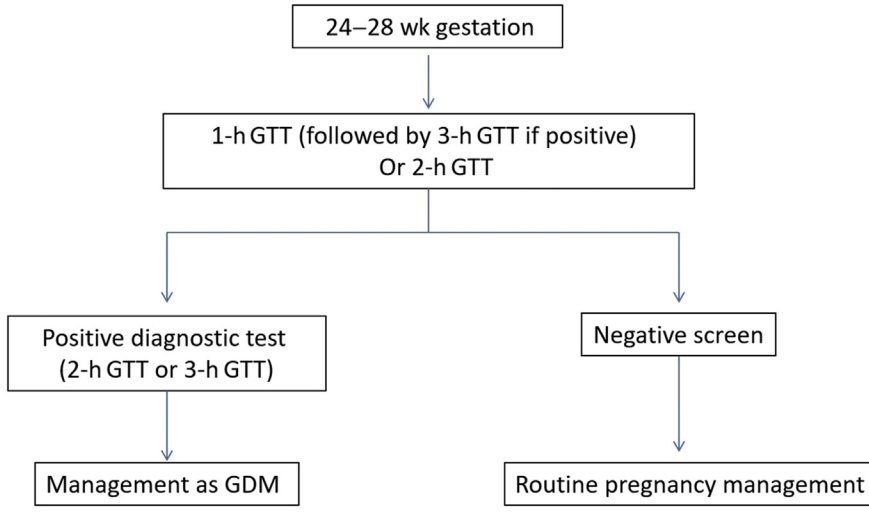

Fig. 2. GDM screening. At-risk patients with negative early screening or low-risk patients with no prior screening.

Box 1
Risk factors for gestational diabetes mellitus

- Glucosuria
- Multiple gestation
- Maternal age greater than 25 years old
- Prior pregnancy affected by GDM
- History of impaired glucose tolerance
- Prior unexplained perinatal loss or child with congenital anomaly
- Hypertension
- Obesity
- Use of glucocorticoids
- Polycystic ovarian syndrome
- Family history of diabetes
- Excessive gestational weight gain
- Significant weight gain in early adulthood
- Intergestational weight retention

Glucose Challenge Tests

The 50-g oral glucose challenge can be taken regardless of fasting or postprandial state with assessment of plasma glucose 1 hour after consumption. The 3 commonly used thresholds for "positive screens" are ≥130 mg/dL (7.2 mmol/L), ≥135 mg/dL (7.5 mmol/L), and ≥140 mg/dL (7.8 mmol/L).[1,2] The USPSTF published a systematic review citing sensitivities and specificities at the low end and the high end for proposed thresholds[2]: 130 mg/dL yielded 88% to 99% sensitivity and 66% to 77% specificity, whereas 140 mg/dL demonstrated 70% to 88% sensitivity and 69% to 89% specificity.[16] In the authors' academic obstetric group, they have adopted a threshold of 135 mg/dL. Upon positive screening, several criteria are used depending on the provider's preference and interpretation of the data's generalizability for implementation in their own population.[16–21] For the 2-step screen ending in a 100-g glucose challenge, Carpenter and Coustan[21] recommend the following cut points (mg/dL): fasting, 95; 1 hour, 180; 2 hours, 155; 3 hours, 140. For the same 100-g challenge, National Diabetes Data Group (NDDG) recommends using the following cut points (mg/dL): fasting, 105; 1 hour, 190; 2 hours, 165; 3 hours, 145.[22] There are others used as well (**Table 2**).

In women with markedly elevated oral glucose challenge screens, a high probability of abnormal diagnostic GTT exists.[23] That being said, the positive predictive value (PPV) depends on both the population's prevalence of GDM and the criteria for diagnosis, for example, NDDG or Carpenter-Coustan.[21–24] Carpenter and Coustan[21] report greater than 95% probability of GDM with 1 hour plasma glucose of greater than 182 mg/dL (10.1 mmol/L) following the 50-g challenge.[21] Other studies report PPV of 200 mg/dL to range from 69% to 80%.[23–25] The authors use 200 mg/dL as a threshold for GDM diagnosis and not requiring exposure to the 100-g GTT. Granted, a patient who prefers the 3-hour GTT in lieu of committing to the diagnosis may do so, as long as the provider is not concerned with risk for clinically significant diabetic ketosis in the patient. Expert opinion has defined

Table 2
Criteria for GDM diagnosis

Plasma Glucose	Carpenter-Coustan (100 gm; Two-Step)	NDDG (100 gm; Two-Step)	CDA (75 gm; Two-Step)	WHO (75 gm; One Step)	IADPSG (75 gm; One Step)
Fasting (mg/dL)	95	105	95	92–125	92–125
One-hour (mg/dL)	180	190	191	180	180
Two-hour (mg/dL)	155	165	160	153–199	153
Three-hour (mg/dL)	140	145	—	—	—

Abbreviations: CDA, Canadian Diabetes Association; IADPSG, International Association of Diabetes and Pregnancy Study Groups; NDDG, National Diabetes Data Group; WHO, World Health Organization.

GDM as diagnosed on GTT by a list of criteria either by the 1-step or by the 2-step approaches (see **Table 2**).[25] The authors' group uses a 2-step approach with the Carpenter-Coustan cut points.[21]

The Eunice Kennedy Shriver National Institute of Child Health and Human Development Consensus Development Conference on Diagnosing Gestational Diabetes recommended the continued use of the 2-step approach to screen for and diagnose GDM.[26] This recommendation was based on the lack of evidence for improved clinical maternal or neonatal outcomes with the 1-step approach (75-g 2-hour GTT) and the increase in health care costs that would result. Based on this recommendation and a *Cochrane Review* that reported no specific screening strategy has shown to be optimal, ACOG supports the 2-step approach.[1,4]

Management (Glucose Monitoring)

Several studies have evaluated the utility of glucose monitoring and treatment of GDM. The 2005 Australian Carbohydrate Intolerance Study in Pregnant Women trial randomized women with GDM to receive treatment or routine care.[27] The study found that treatment was associated with a reduction in serious newborn complications, preeclampsia, and frequency of large for gestational age (LGA) infants. A subsequent randomized controlled trial done in the United States showed a decrease in frequency of LGA infants, reduced neonatal fat mass, and decreased rates of cesarean delivery, shoulder dystocia, and hypertensive disorders of pregnancy with treatment of GDM.[28] Given these observed benefits with treatment, it is recommended that patients monitor their glucose levels, and treatment should be initiated upon diagnosis as appropriate.

Home serum glucose monitoring is the crux of outpatient maternal surveillance with GDM. Patients are routinely instructed on glucometer use and the importance of steadfast maintenance of a glucose log as derived from fasting and either 1-hour or 2-hour postprandial glucose levels.[1] Such monitoring facilitates ease of review by the patient's obstetric provider and in the identification of deviations from target glycemic measures. In patients with poor control, providers may additionally ask patients to monitor preprandial glucose levels, whenever sensing high or low glucose, and at 2 to 3 AM in the morning to better characterize the overall control of the patient's glucose throughout the day. Current standard of care for target blood glucose values are fasting blood glucose concentration $\leq$95 mg/dL (5.3 mmol/L), 1-hour postprandial blood glucose concentration $\leq$140 mg/dL (7.8 mmol/L), and 2-hour postprandial glucose concentration $\leq$120 mg/dL (6.7 mmol/L) (**Fig. 3**).[1,28]

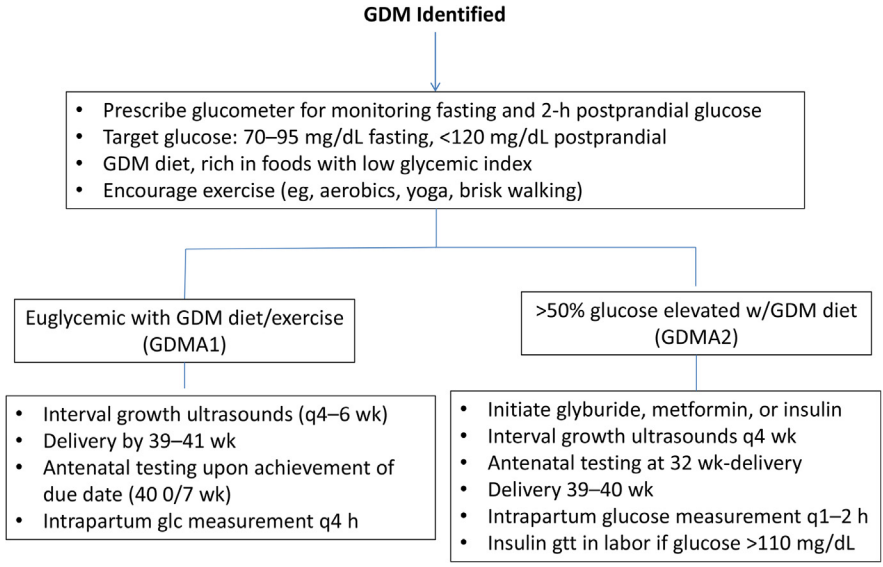

Fig. 3. GDM identified. Rx, prescription; u/s, ultrasound.

Management (Diet Control)

Dietary changes are the mainstay of initial attempts in glycemic control following the diagnosis of GDM. Data demonstrate a clear association of postprandial hyperglycemia and diet high (>55%) in carbohydrate content.[28,29] Because carbohydrates are the sole macronutrient to significantly raise postprandial blood glucose, dietary modification predominantly consists of carbohydrate restriction and distribution evenly throughout the 3 main meals of the day.[30,31] Glycemic control is improved by avoiding processed/red meat, high-fat dairy, refined grains while favoring vegetables, fruit, whole grains, and fish[31–36] (**Box 2**). For patients achieving target measures for glucose control with GDM diet, the diagnosis remains diet-controlled GDM or GDMA1 per the widely used White Classification that stratifies diabetes by pregestational diabetes mellitus (DM) with or without organ involvement and GDM, either controlled by diet alone or requiring medication.[37] Some patients will consistently demonstrate fasting blood glucose greater than 100 mg/dL along with a persistent pattern of postprandial glucose measures greater than 120 mg/dL despite the GDM diet; these patients

Box 2
Gestational diabetes mellitus diet

- Review IOM guidelines for weight gain as based on patient's BMI
- Limit carbohydrates to 40% to 45% of calories
- Avoid processed sugar (eg, soda, candy)
- Avoid fruit and juice at breakfast
- Encourage increased fiber intake and foods with low glycemic index
- Move fruit and milk servings to snack time
- Keep starchy carbohydrates at meal
- Encourage exercise plan

require medical therapy and have GDMA2.[30,37] Some of these patients may have occult diabetes simply diagnosed during pregnancy and may also fail to achieve euglycemia with institution of the GDM diet.

Recently, investigators have evaluated the impact of a diet with low glycemic index (GI) for improvement of outcomes in GDM.[29] The GI is a systematic and physiologically based measurement of the dietary carbohydrate load and its inherent glycemic burden.[30] GI is the number associated with the carbohydrates in a particular type of food, indicating the individual's response (assessed by blood sugar level) relative to the reference food—pure glucose.[30–34] High GI diets result in more gestational weight gain, whereas low GI foods are associated with lower birth weight, improved insulin sensitivity, and potentially lowered risk for development of GDM, better adherence to Institute of Medicine (IOM) weight gain guidelines in pregnancy, and lower onset of obesity later in life.[29–36] Low GI diet effectively reduces postprandial blood glucose spikes, appears to be safe in pregnancy, and shows promise for improving the outcomes with GDM.[34–36]

Gestational Weight Gain and Gestational Diabetes Mellitus

Because obesity and insulin resistance parallel one another in terms of comorbidity, the 2 conditions are somewhat inseparable in terms of clinical considerations. Both, if not well controlled, lead to increased risk of indicated preterm delivery, gestational hypertension, preeclampsia, delivery by cesarean, and fetal growth abnormalities.[1,2,26–28] Excessive gestational weight gain correlates well with onset of GDM.[38] Accordingly, 2009 IOM Guidelines for weight gain in pregnancy provide direction for target weight gain as based on intake body mass index (BMI).[39] Online calculators based on IOM guidelines to individualize the approach are available.[40] Regardless of BMI, a typical goal for a patient's calorie intake would be 30 to 35 calories per kilogram ideal body weight. Five hundred of those daily calories should be protein (125 g).[41] The remainder of the calories may then be equally halved between fat and carbohydrate while avoiding processed carbohydrates. A good recommendation for calorie distribution by meal would be 24% at breakfast, 30% at lunch, 33% at dinner, and the remaining 13% from between-meal snacks.[41] Keeping gestational weight gain to within the IOM guidelines can reduce the risk of developing GDM and improve glycemic control in women with GDM.[29–35,38,41]

Management (Pharmacologic Control: Oral Hypoglycemic Agents and Insulin)

When diet fails to achieve euglycemia, defined as no more than 50% of glycemic measures above the target ranges, medication is required and the patient is classified as GDMA2.[1,36] Both oral hypoglycemic agents and insulin therapy are acceptable and used. Insulin therapy has been the most well-studied and used treatment of both GDMA2 and DM and continues to be endorsed by the ADA and ACOG as an accepted therapy.[1] Insulin does not cross the placenta and is the only regimen approved by the US Food and Drug Adminstration for treatment of GDM.[1] Insulin regimens typically consist of a long-acting and a short-acting insulin; however, insulin dosing and regimens must be individualized. Given that insulin resistance increases with increasing placental mass, total insulin requirements increase with increasing gestational age. A commonly used protocol uses maternal weight and gestational age to calculate starting daily insulin requirements (**Table 3**).[1] The total daily insulin requirement is then divided into two-thirds long-acting and one-third short-acting insulin. The short-acting insulin (one-third of total dose) is further subdivided into 3 doses taken with meals.[1] Commonly used long- and short-acting insulins are listed in **Table 4**.

In addition, close surveillance of glucose values is also indicated in patients with GDM who are receiving a course of antenatal corticosteroids for fetal lung maturity.

Table 3
Weight-based guidelines for starting/adjusting total daily insulin therapy by gestational age

Weeks Gestational Age	Insulin (Units/kg/d)
0–13 6/7	0.7
14–27 6/7	0.8
28–35 6/7	0.9
36–delivery	1.0

Corticosteroids are known to increase the risk of transient hyperglycemia, thus more frequent assessments of maternal glucose in this setting (eg, every 4 hours depending on initial starting glucose level) are appropriate.[42] In the setting of post–corticosteroid hyperglycemia, patients often require insulin coverage even if they were previously well controlled with diet.[43]

Oral Hypoglycemic Agents

Commonly used oral hypoglycemic agents include both glyburide and metformin. Glyburide is a second-generation sulfonylurea that was investigated using single-cotyledon placental models to assess placental transfer. Initial studies demonstrated no significant transfer of glyburide in both therapeutic and supratherapeutic dosing concentrations.[44,45] The subsequent landmark randomized controlled trial compared the insulin therapy to glyburide in the management of GDM. Not only was there no detectable glyburide in cord blood but also maternal and neonatal outcomes were similar with respect to glycemic control and adverse events.[46] Notably, subsequent data conflict the initial Langer randomized controlled trial reporting glyburide being actively transported from the fetus to the mother.[47] Although the range of fetal exposure varied widely, 9% to 70% maternal glyburide concentration, these data create pause for consideration of possible fetal risks. A 2015 meta-analysis showed therapeutic glyburide use resulted in a 2-fold increase in neonatal hypoglycemia, a 2-fold increase in macrosomia, and a 100-g increase in mean birth weight compared with traditional insulin therapy.[47] In addition, 4% to 16% of women who took glyburide as initial therapy eventually required the addition of insulin.[1,47]

Metformin is a biguanide used to improve both fertility and glycemic control by way of increasing insulin sensitivity.[48] Insulin sensitivity is heightened by metformin via an inhibitory effect on hepatic glucose production and intestinal glucose absorption.[48] Pharmacologic studies demonstrate that metformin freely crosses the placenta, rendering a circulating fetal concentration roughly 50% that found in maternal circulation.[48] Accordingly, a landmark trial published by Rowan and colleagues[49] called the Metformin in Gestational Diabetes (MIG) trial compared the outcomes of 751 women and fetuses allocated to either traditional insulin therapy or metformin for the treatment of GDM. Although there were no differences in congenital malformations, serious

Table 4
Long- and short-acting insulins used for gestational diabetes mellitus treatment

Long Acting	Short Acting
Glargine (Lantus)	Aspart
Protamine Hagedorn (NPH, Novolin)	Lispro
Detemir	Regular

maternal events, or serious neonatal events, significant variance in outcome was shown with use of metformin. Namely, metformin use resulted in significantly less neonatal hypoglycemia (3.3% vs 8.1%; $P<.008$) and an unexpected higher rate of preterm delivery (12.1% vs 7.6%; $P = .04$). A 2-year follow-up report on the MIG trial babies showed those in the metformin arm had more subcutaneous fat in upper arm and shoulder compared with those in the insulin arm.[50] In addition, 26% to 46% of patients who took metformin alone eventually required insulin.[50]

Although insulin therapy remains the standard therapy recommended by most, oral antihyperglycemic agents are a reasonable alternative in patients who refuse to take or are unable to comply with insulin therapy. Providers should have a thorough discussion of the published outcome data and unknown long-term effects of transplacental passage of oral agents.[1]

Fetal Surveillance

Given the effect of hyperglycemia on fetal growth and well-being, women diagnosed with GDM are typically followed with serial biometry and amniotic fluid volume assessment. Frequency of such assessments is typically performed every 4 to 6 weeks from time of diagnosis of GDM to delivery. Indications for antepartum fetal testing include insulin or oral hypoglycemic requirement, polyhydramnios, onset of gestational hypertension, or, less commonly in the setting of GDM, growth restriction. Although a consequence of poorly controlled GDM, testing is not indicated for macrosomia. Either weekly biophysical profile or twice weekly nonstress tests with weekly amniotic fluid indices after 32 weeks are acceptable and equivalent for ensuring fetal well-being when indicated (see **Fig. 3**).[1] There is currently no consensus regarding antepartum fetal testing for women with GDMA1 because studies have not demonstrated an increased risk of stillbirth in these patients before 40 weeks.[1,49,51]

Intrapartum Management and Delivery Timing

Provided glucose measures demonstrate good control with diet alone and serial ultrasound demonstrates normal growth and amniotic fluid volume, the patient essentially has uncomplicated GDMA1 and does not require timed delivery before 41 weeks 0 days. Notably, ACOG does allow for the role of elective delivery in term patients with good dating following the achievement of 39 weeks' gestational age.[51,52] Hence, timing for delivery in those who are term albeit less than 41 weeks can be individualized with patient and the obstetric provider. Upon surpassing the due date, a good practice would be to initiate antenatal testing and weekly amniotic fluid volume measurements. On the contrary, patients with GDMA2 are likely best served by delivery at 39 0/7 to 39 6/7 weeks of gestation given increased risk of stillbirth in patients who require insulin or oral hypoglycemic medication for glucose control.[50,51] Moreover, recent data indicate inducing labor actually does not increase risk for cesarean delivery and that induction at 39 weeks yields lower failure rate (as defined by cesarean) than induction at 40 or 41 weeks.[53,54] In women with poor glycemic control despite medical intervention, delivery before 39 weeks may be warranted. Recommendations for delivery timing should incorporate consideration for risks of prematurity and ongoing risk of stillbirth (see **Fig. 3**).[1,55]

Delivery Mode

Simply stated, GDM is not an indication for cesarean delivery. That being said, GDM places a fetus at greater risk for macrosomia as defined by an estimated fetal weight (EFW) in excess of 4500 g for pregnancies affected by GDM/DM per the

most recent ACOG Practice Bulletin.[1] In addition, fetuses often show an accelerated growth pattern with abnormally low head circumference/abdominal circumference ratio even in the absence of macrosomia. These growth patterns are important risk factors for complications, such as shoulder dystocia, Erb palsy, and third/fourth degree lacerations.[56–58] Scheduled cesarean section is typically offered to women with GDM whose fetuses are estimated to be ≥4500 g.[1] Risks of birth trauma, shoulder dystocia, errors in estimating fetal weight, and risks of cesarean section both immediate and for future pregnancies should be included in the counseling. In women undergoing a trial of labor, caution should be exercised in the second stage especially in the scenario of an operative vaginal delivery because even appropriately grown fetuses of mothers with GDM are at increased risk of shoulder dystocia.[1,56–58]

Insulin Glucose Tolerance Test Protocol and Glycemic Monitoring Protocol Intrapartum

Given that labor increases glucose utilization, hyperglycemia in women not requiring medical control of GDM is rare. Hence, practitioners may periodically monitor glucose every 4 hours intrapartum for GDMA1.[1,58] On the contrary, gestational diabetics requiring either oral hypoglycemic medications or insulin (GDMA2) respond similarly to DM in labor and are best served by every 1- to 2-hour glucose assessments in the intrapartum period. Although ketoacidosis is rare in GDMA2, intrapartum maternal hyperglycemia may cause an acute increase in fetal insulin, placing the fetus at heightened risk for neonatal hypoglycemia.[58] The authors' group initiates an insulin drip upon maternal blood glucose at or greater than 120 mg/dL, with the addition of D5 (dextrose 5%) ½ NS (normal saline) at 125 cc/h provided glucose levels are less than 200 mg/dL. Similarly, in a survey of academic medical centers, 60% aimed to maintain maternal glucose less than 110 mg/dL, whereas 30% targeted a value between 110 and 150 mg/dL.[1,42]

Postpartum Screening

Many women with GDM are pregestational diabetics that were first detected in pregnancy, and women with true GDM are at risk for the development of DM later in life.[59,60] Seventy percent of women with GDM will develop DM at some point in their life, and 40% to 50% of those women will develop DM within 10 years.[61] Hence, all women should receive screening for DM with a 75-g GTT at 6 to 12 weeks postpartum. If negative, they should continue to be rescreened every 3 years with their primary care provider.[61] Women with a positive 2-hour GTT are diagnosed with DM and should be managed or referred for long-term management accordingly.[61]

Encouraging breastfeeding, regular physical activity, and formal nutrition programs focusing on decreased gestational weight retention are recommended by the ADA.[59–61] However, given that 44.9% of US births are covered by Medicaid and many of these women experience coverage lapses due to Medicaid coverage ending at 60 days' postpartum, cost becomes an issue. Research shows that obstetricians have much room for improvement in their rates of nutrition referrals and postpartum screening for patients who had GDM.[59–61] Unfortunately, women seeing a primary care physician after delivery often fail to disclose the fact their recent pregnancy was complicated by GDM.

Martinez and colleagues[61] recently recommended Situation Background Assessment Recommendation strategy to help bridge the gap between GDM and postpartum care. This model reinforces recommendations through reminders to both patient and provider to facilitate communication, screening, and care (**Box 3**).

Box 3
Postpartum management and situation background assessment recommendation

- Discontinue insulin or oral hypoglycemic
- Encourage breast-feeding
- Encourage enrollment in formal exercise program or encourage exercise as patients progress through convalescence and recovery in the puerperium
- Encourage referral to formal nutrition program
- Routine contraceptive recommendations (no change based on GDM)
- 75-g GTT at 6 to 12 weeks' postpartum
- "Warm handoff" to primary care provider replete with notification of pregnancy complication by GDM
- Repeat 75-g GTT every 3 years until positive (then manage as DM)

SUMMARY

GDM is a common complication in pregnancy. Risks associated with occult or unmanaged GDM are detrimental to both maternal and fetal well-being. Sufficient evidence exists to warrant screening and management strategies once diagnosed. Although many variations in both screening and management may be reasonable, the authors suggest a few key points for optimizing identification and management of GDM.

For patients at increased risk for insulin resistance, they recommend an early screen, either the 2-hour GTT or 2-step (1-hour followed by 3-hour GTT if positive). Should patients have a positive diagnostic test before the achievement of 20 completed weeks' gestation, the authors recommend management as pregestational DM. On the contrary, the at-risk patient with an initial negative screen before 20 weeks should then be rescreened at the usual 24- to 28-week gestational age window (see **Fig. 1**).

For either at-risk patients with negative early screening or low-risk patients with no indication for early screening, the authors recommend screening with either the 1-hour GTT (followed by 3-hour GTT if positive) or 2-hour GTT for diagnosis. Patients exhibiting a negative screen may have routine pregnancy management. Patients with a positive diagnostic test (by either 2- or 3-hour GTT) should be managed as GDM in their pregnancy (see **Fig. 2**).

When GDM is identified, the authors recommend the following:

1. Glucometer for monitoring fasting and 2-hour postprandial glucose;
2. Target glycemic measures of 70 to 95 mg/dL (fasting) and less than 120 mg/dL (postprandial);
3. GDM diet;
4. Diet risk in foods with low GI; and
5. Encourage exercise (eg, aerobics, yoga, brisk walking) (see **Fig. 3**).

Provided GDM patients achieve euglycemia with diet and exercise (GDMA1), the authors recommend interval growth ultrasounds (every 4–6 weeks); delivery 39 to 41 weeks; antenatal testing upon achievement of 40 completed weeks; and, intrapartum glucose measurement every 4 hours. For patients with more than half of their glucose measurements elevated despite GDM diet (GDMA2), the authors recommend the following: initiation of glyburide, metformin, or insulin; interval growth ultrasounds every 4 weeks; antenatal testing from 32 weeks until delivery; delivery from 39 to

40 weeks; intrapartum glucose measurement every 1 to 2 hours; and initiation of insulin drip in labor if glucose is at or greater than 110 mg/dL. Last, the authors recommend following ACOG guidelines regarding an adequate discussion of risks for birth injury should EFW exceed 4500 g (see **Fig. 3**). As a good clinical practice, the authors' group exhibits caution with assisted second-stage deliveries when EFW exceeds 4250 g (ie, if spontaneous delivery cannot be facilitated by maternal expulsive efforts, the authors recommend consideration for cesarean section at this point in lieu of using either forceps or vacuum in this setting, which may facilitate an undesired outcome, shoulder dystocia).

Last, postnatal testing of GDM patients should be performed to ensure that patients who actually have DM are identified. If initially negative, women with history of GDM should be rescreened every 3 years. Warm handoffs to primary care providers with these recommendations should help facilitate better rates of screening for those at risk for DM and in turn help identify occult DM so that women receive treatment when appropriate.

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