Gestational Diabetes Mellitus: What Else Is New?

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Screening, diagnosis and classification

Gestational diabetes mellitus is defined as glucose intolerance that is first detected during pregnancy [1]. Depending on the ethnic group and diagnostic criteria of the population studied, the occurrence of gestational diabetes ranges between 1.4% and 14.0% [2]. Although evidence suggests that even mild maternal hyperglycemia increases fetal morbidity, it occurs only in a minority of cases, rendering routine GDM screening questionable [3]. In contrast, failure to recognize GDM might result in greater fetal or maternal morbidity. Because GDM is usually asymptomatic, we have to rely on various screening programs to select patients for the 3 hour diagnostic oral glucose tolerance test (100 g). In 1998 the fourth international workshop-conference on gestational diabetes [1] recommended universal GDM screening of all pregnant women, using the 50 g glucose challenge test at 24–28 weeks gestational age. A cutoff of 140 mg/dl (7.8 mmol/L) on the GCT (which identifies approximately 80% of women with GDM) was agreed upon for requiring OGTT. The detection rate is increased to 90% using a cutoff of >130 mg/dl (7.2 mmol/L), but this cutoff is associated with more false positive results, requiring more women to unnecessarily undergo OGTT. In contrast, the American Diabetes Association adopted a selective screening program, which uses risk assessment at the first prenatal visit to determine the necessity of GDM screening [2] [Table 1]. The ADA established two diagnostic criteria for OGTT: the 100 g OGTT with Carpenter and Coustan's modification [4] of O'Sullivan and Mahan's criteria [5] or the 75 g OGTT [Table 2]. However, for detection of infants or mothers at risk, the 75 g criterion is not superior to the 100 g OGTT. The GDM screening controversy is best exemplified by the recently published statement of the U.S. preventive services task force, concluding that there are insufficient data to recommend for or against routine screening for GDM since they found no solid evidence that screening for GDM substantially reduces important adverse health outcomes for mothers or their infants [6,7].

Table 1. Risk factors for gestational diabetes mellitus

- Family history of diabetes
- Increasing maternal age
- GDM in previous pregnancy
- Overweight
- Prior infant ⩾ 4,500 g
- Previous stillbirth
- Ethnic group with high prevalence of diabetes
- Polycystic ovarian syndrome

Table 2. ADA diagnostic criteria of diabetes during pregnancy (glucose measured in plasma or serum by a high precision method)

Time	Diabetes 1 or 2	GDM
Random sampling *, **	⩾ 200 mg/dl (11.1 mmol/L)	–
Overnight fast**	⩾ 126 mg/dl (7.0 mmol/L) ***	95 mg/dl (5.3 mmol/L)
1 hour GTT ***		180 mg/dl (10.0 mmol/L)
2 hour GTT ***		155 mg/dl (8.6 mmol/L)
3 hour GTT ***		140 mg/dl (7.8 mmol/L)

* Except during GCT and GTT

** Should be present on at least two occasions or with 75 g GTT.

*** Positive test = 2 or more values equal or higher than these.

Either a 2 hour (75 g glucose) or 3 hour (100 g glucose) can be performed.

Obstetric and perinatal effects and considerations

Early effects of GDM

Maternal adverse health outcomes of GDM associated with pregnancy include increased rates of cesarean delivery [3], increased rates of preeclampsia [8], and alterations in obstetric management due to caregiver bias [3,8,9]. Other than macrosomia, adverse health effects of gestational diabetes on the neonate are less consistent. However, there is evidence supporting the association between maternal gestational diabetes and preterm birth, neonatal hypoglycemia, hyperbilirubinemia, hypocalcemia, and polycythemia. Importantly, the presence of maternal fasting hyperglycemia (> 105 mg/dl) may be associated with an increased risk of intrauterine fetal death during the last 4–8 weeks of gestation [2]. Another disturbing complication recently reported by Moore et al. [10] is that women with gestational diabetes were 7.7 times as likely (95% confidence interval 2.8–21.1) to have an infant with a numeric sex chromosome defect as those without gestational diabetes. However, it is not clear how many women in this study had undiagnosed pregestational diabetes, a known risk factor for chromosomal anomalies.

Long-term effects of GDM

The long-term implications for mothers with GDM include a higher

GDM = gestational diabetes mellitus
GCT = glucose challenge test
OGTT = oral glucose tolerance test
ADA = American Diabetes Association

risk for developing type 2 diabetes mellitus, with an excess risk of 18–32%, compared to women without GDM [11]. Furthermore, having a second pregnancy complicated by GDM amplifies the risk of type 2 diabetes mellitus during 7 years of follow-up by 2.5 times than in women who had GDM only once [12]. In a population-based study of more than 140,000 women [13], those whose mothers had had diabetes (of any type) during pregnancy were at increased risk of gestational diabetes with an adjusted odds ratio of 9.3 (95% CI 4.1–21.1). Several studies suggested that the diagnosis of maternal GDM may have long-term implications for the offspring, such as an increased risk for impaired glucose tolerance, childhood obesity, and neuropsychological disturbances. These may be related to the severity of the maternal hyperglycemia during pregnancy, third-trimester maternal lipid metabolism disturbances and fetal hyperinsulinemia [14–16].

Management

Diet

Diet is the mainstay of therapy for patients with GDM. Diet should be individualized, considering maternal body mass index, the individual's physical activity and dietary preferences. Maternal glucose levels should be consistent with the recommended goals for diabetic control [Table 3]. A 30–33% caloric restriction is recommended for obese women (BMI >30 kg/m^2). Carbohydrate reduction to 35–40% of calories has been shown to decrease maternal glucose levels and improve both maternal and fetal outcomes. This diet has been shown to reduce hyperglycemia and plasma triglycerides with no increase in ketonuria [17].

Exercise

To optimize pregnancy outcome, up to 39% of patients with GDM will require insulin therapy [18]. However, the need for insulin was decreased when a 45 minute session of moderate aerobic exercise was performed at least three times a week in a supervised controlled manner [19]. Moreover, exercise is associated with reduced rates of GDM among women with BMI greater than 33 (OR 1.9, 95% CI 1.2–3.1) [20].

Insulin therapy

When diet and exercise fail to achieve the required glucose level goals, insulin therapy is recommended. Blood glucose levels should guide the proper doses and timing of the insulin regimen. Two approaches are commonly used to identify women whose fetuses are at sufficiently high risk to warrant more intensive therapy: one involves frequent self-monitoring of blood glucose to identify hyperglycemia [21] and the other is to sonographically assess fetal macrosomia [22]. The most common approach and the one backed by the greatest clinical experience uses intensive SMBG [1,2,21]. Using stricter glycemic targets than mentioned in Table 4 without pre-selection for mothers with large fetuses [23] may increase the rate of delivery of small for gestational age infants [21].

CI = confidence interval
BMI = body mass index
OR = odds ratio

Table 3. Postpartum 75 g OGTT (ADA criteria)

Normoglycemia	IFG and IGT	Diabetes mellitus
FPG < 110 mg/dl	FPG = 110–125 mg/dl	FPG ⩾ 126 mg/dl
2 hr < 140 mg/dl	2 hr = 140–199 mg/dl	2 hr ⩾ 200 mg/dl
		Symptoms and random ⩾ 200 mg/dl

IFG = impaired fasting glucose, IGT = impaired glucose tolerance, FPG = fasting plasma glucose.

Table 4. Glucose level goals – fasting and postprandial

Medium	Fasting	1 hr postprandial	2 hr postprandial
Whole blood	⩾ 95 mg/dl (5.3 mmol/L)	⩾ 140 mg/dl (7.8 mmol/L)	⩾ 120 mg/dl (6.7 mmol/L)
Plasma	⩾105 mg/dl (5.8 mmol/L)	⩾ 155 mg/dl (8.6 mmol/L)	⩾ 130 mg/dl (7.2 mmol/L)

Oral glucose-lowering agents

Langer et al. [24] found a similar perinatal outcome in a randomized unblinded clinical trial that compared the use of insulin versus glyburide after the first trimester in women with GDM who were not able to meet the glycemic goal. However, although promising, glyburide has not been approved by the U.S. Food and Drug Administration for the treatment of GDM, and further studies in a larger population are needed to establish its safety [2].

Delivery

The rate of cesarean section among women diagnosed with GDM is more than double that among non-diabetic women [25]. The increased rate is partly attributed to fetal macrosomia but it may be confounded by physicians' bias when caring for women with known GDM [9]. The mode of delivery in well-controlled women should be based on obstetric indications. Timing of delivery on the other hand is a complex issue. In a study of women with insulin-treated diabetes (93% of whom had gestational diabetes), Kjos et al. [26] showed that routine induction of labor at 38 completed weeks, in the absence of maternal or fetal jeopardy, resulted in fewer infants who were large for gestational age (10% vs. 23%). Induction of labor was associated neither with increased rate of cesarean delivery (25 vs. 31% among women who were not induced) nor with shoulder dystocia (0 vs. 3%). Prior to 38 gestational weeks, the indication for preterm delivery should dictate whether assessment of fetal lung maturity is warranted [1].

Post-pregnancy care

Children born to mothers who had poor glycemic control should undergo regular evaluations of height, weight and blood glucose concentration, as well as monitoring for appropriate physical activity and diet to minimize the likelihood of obesity [1]. The likelihood of women with GDM to develop diabetes mellitus is 17–63% and is particularly high in women who have marked hyperglycemia during or soon after pregnancy [27–29]. Obese women [27,28] and women whose gestational diabetes was diagnosed before 24 weeks of gestation [29] also have an added

SMBG = self-monitoring of blood glucose

increased risk for diabetes mellitus later in life. These facts make GDM a unique opportunity for the healthcare provider to diminish insulin resistance by encouraging exercise and maintenance of normal weight. According to the ADA, blood glucose concentrations should be assessed after delivery complicated by GDM, and at least every 3 years thereafter. Impaired fasting or post-challenge blood glucose levels warrants more frequent testing. It is also important that women with previous GDM use effective contraception to minimize the chance of pregnancy with untreated hyperglycemia, which increases the risk of birth defects in their infants. Low dose oral contraceptives were not found to increase the risk of developing overt diabetes, whereas a progestin-only oral contraceptive is best avoided by breast-feeding women with prior GDM because it may be associated with a threefold increase in the risk for developing overt diabetes [30].

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If I could live this life again, I'd do exactly the same except I wouldn't read Beowulf

Woody Allen