

Gestational Diabetes: A Conundrum for Mother, Baby and Physician

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There are nearly 4 million births in the United States each year and in approximately 6% (240,000) of those pregnancies there will be some kind of glucose intolerance. In about 10% of these the diagnosis of diabetes will antedate the pregnancy. The remaining 90% will have gestational diabetes; or glucose intolerance discovered only during pregnancy [1]. Poor maternal glucose control during the first eight weeks of pregnancy, with subsequent hyperglycemia and lipid peroxidation, can have severe implications for the fetus including birth defects [2]. It is well known that, in the USA, congenital anomalies are the leading cause of infant death [3] (Mathews & MacDorman. Natl Vital Stat Report 2010; 58:1). Likewise, other risks to the newborn from maternal diabetes include shoulder dystocia, respiratory distress syndrome, macrosomia and metabolic derangement, any of which may lead to a costly admission to the neonatal intensive care unit [4]. Similarly, maternal risks of diabetes include increased rates of labor induction, abdominal delivery, infection, hypertension and diabetic ketoacidosis [5]. Finally, women with diabetes also have a life expectancy 12.9 years lower than women without diabetes [6].

If that's the bad news, the good news is that women with diabetes (pre-existing and gestational) can have near normal pregnancies with little increase in morbidity if glucose excursions are well controlled throughout pregnancy [7]. This statement presupposes that women who will develop gestational diabetes can be diagnosed and treated early in pregnancy. Accordingly, if women with known diabetes have preconception counseling and a planned pregnancy, intervention can lead to tight glucose control before gestation and during the crucial period of organogenesis thus reducing birth defects. In addition, if glucose excursions are well controlled throughout pregnancy neonatal complications such as macrosomia/large for gestational age status, shoulder dystocia and respiratory/metabolic complications may be ameliorated [4]. Importantly, tight glucose control before/during pregnancy may help avoid the metabolic syndrome in children (Figure 1). It has been demonstrated that the metabolic syndrome risk is approximately 50% when a large for gestational age infant is the product of a pregnancy with maternal gestational diabetes [8].

Traditionally, the screening and diagnosis of gestational diabetes in the United States is a two-step process and is performed at 24 to 28 weeks of gestation. The process begins with a random 50 gram oral glucose load followed by a one hour plasma glucose determination [1]. If the screening result is greater than or equal to 140 mg/dl the diagnostic test, typically a fasting 100g oral glucose tolerance test with plasma glucose levels determined at fasting, one-hour, two-hour, and three-hour intervals, is performed. Two abnormal (elevated) levels will herald the diagnosis of gestational diabetes. To address the issue of early diagnosis, the International Association of Diabetes and Pregnancy Study Group (IADPSG) [9] recommended two paradigm shifts. First, all patients should be screened for hyperglycemia at the first prenatal visit either using a hemoglobin A_{1c} or fasting plasma glucose. If the fasting level is ≥ 92 mg/dl, ≥ 5.1 mmol/l but, <126 mg/dl is <7.0 mmol/l a diagnosis of gestational diabetes is made. This will result in more women being diagnosed with gestational diabetes earlier than the 24-28 week period thus allowing more time to control glucose excursions [9]. Secondly, in those with a normal test result, a

75 gram glucose tolerance test is used for diagnosis using lower plasma thresholds and only one abnormal value being required to diagnose gestational diabetes (≥ 92 mg/dl fasting; ≥ 180 mg/dl – 1 hour; ≥ 153 mg/dl – 2 hour; Table 1); the one-step approach.

The vast majority of obstetricians in the United States have not adopted the IADPSG [6] policy because, to date, there is no consensus that the diagnosis of more women with diabetes (12.9% - two-step method versus 37.7% - one-step method) will result in improved maternal-fetal outcomes [10,11]. Such data is just starting to accumulate. Landon et al. [4], has shown that if the fasting blood glucose is greater than 90 mg/dl and 1-hour greater than 165 mg/dl, there is more neonatal morbidity. If the 1-hour is greater than 150 mg/dl there is also an increase in large for gestational age infants. Further,

METABOLIC SYNDROME IN CHILDHOOD

- Metabolic syndrome diagnosed when three of five categories met
 - Obesity
 - Hypertension
 - CHO intolerance
 - Low HDL
 - Hypertriglyceridemia

Figure 1: Metabolic syndrome in childhood.

Glucose Diagnostic Levels for Gestational Diabetes	Fasting*	1-hour	2-hour	3-hour
Carpenter/Couston ^o	95	180	155	140
National Diabetes Data Group (NDDG) ^o	105	190	165	145
International Association of Diabetes + And Pregnancy Study Group (IADPSG_)	92	180	153	---

*mg/dl,

^oTwo step method (50gm oral load – 1 hour glucose) – If >140 mg/dl, a 3 hour glucose tolerance test is performed

*One step method (75gram oral load followed by 2 hour GTT)

Table 1: Diagnostic Criteria for Gestational Diabetes.

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Mayo et al. [12] have shown that when the two modes of testing were compared, there was an increase in the diagnosis of gestational diabetes with the one-step 75 gram oral GTT method. However, both testing modalities had increased Cesarean delivery rates as well as increases in large for gestational age infants and composite neonatal morbidity demonstrating that the additional women diagnosed with gestational diabetes were also at an increased risk for adverse outcome. Fong et al. [13] have shown that using a hemoglobin A_{1c} of greater than 6.5% (which is currently the standard) at the first prenatal visit is more sensitive than the 1-hour oral glucose load in screening for gestational diabetes. However, when the level of hemoglobin A_{1c} is reduced to a cut point between 5.7% and 6.4%, 27.3% were diagnosed gestational diabetes compared to 8.7% if the hemoglobin A_{1c} cut off was <5.7%. This increase in diagnosis remained after statistical adjustment for maternal age, body mass index, ethnicity and gestational age.

In contrast, it has been pointed out by several national groups and major editorials in major journals in the United States that just because we can make more frequent diagnoses of gestational diabetes, doesn't make it right [1,11,14- 17]. At present, using Level 1 data, it has not been confirmed that the more frequent diagnosis of gestational diabetes has translated into better maternal, fetal, and neonatal outcomes. There are other problems, as well. In parts of the United States there is a critical shortage of physicians and nurses (in addition to dietitians and diabetes educators). The 18% increase in cases of gestational diabetes would produce a serious strain on medical manpower [17]. Also, the IADPSG recommendations have been found to be cost effective only when the patients receive additional prenatal monitoring as well as counseling and education in behavior modification [18]. Consideration should also be given to the concern that the new diagnostic criteria may inappropriately designate women with mild degrees of hyperglycemia as having diabetes and this could have significant personal consequences such as unnecessary testing or an altered insurance rating. The additional cases of gestational diabetes could also portend an increase in the obstetrician's medicolegal profile [17]. Therefore, in the United States, it appears that more Level 1 evidence is required as well as evaluation of long-term outcomes in both groups before the new paradigm can be placed into practice [19]. Clearly only time will tell regarding which testing schema will prove best for all concerned.

Why have we not seen an overall change in morbidity and mortality when gestational diabetes is diagnosed? Principally, our problem seems to revolve around the difficulties in achieving "tight" control of glucose excursions in pregnancy. Obviously, blood glucose levels after meals are affected by the triad of diet, exercise and medication. Even in the most stable patient, it is difficult to balance these three factors in order to control glucose during the entirety of the gestation. Optimal glycemic control is shown on Table 2 and is usually evaluated in patients with gestational diabetes by fasting glucose and either pre- or post-meal testing. For many with gestational diabetes, appropriate glucose control can be achieved effectively by diet alone or with oral hypoglycemic agents such as biguanides (metformin) or sulfonylureas (glyburide) [20]. The best results are usually achieved when a motivated patient has access to frequent telephone contact with a dietician and/or a nurse skilled in diabetes (with the appropriate physician supervision). For women who continue to have difficulty with glucose control, insulin may be substituted for the oral agents when fasting blood glucose is ≥ 100 mg/dl, hemoglobin A_{1c} $\geq 6.0\%$, or 2-hour post-prandial blood glucose is persistently ≥ 120 mg/dl. An insulin with intermediate duration of such as NPH is usually combined with regular or a rapid

acting insulin and both are given in split doses, 2/3 in the AM and 1/3 in the PM to achieve tight glucose control (Table 2).

Post-partum glycemic assessment is also important. It is our policy to check fasting or random plasma glucose 1-3 days after delivery to detect abnormal glucose levels (fasting ≥ 100 mg/dl, random ≥ 140 mg/dl). Around the time of the first post-partum visit (approximately six weeks) a fasting plasma or 2-hour post-prandial glucose level is performed. If the result is normal then the glycemic status should be assessed every three years with diet and exercise counseling, as required. If there is impaired fasting glucose (≥ 100 mg/dl) or impaired- glucose tolerance (≥ 140 mg/dl) or both, patients typically receive intensive dietary counseling. If this does not result in excellent glucose control then oral agents can be added. If this results in good control then oral medications are continued with frequent assessment of glycemic status (Figure 2). If oral agents do not result in good postpartum control, the diagnosis of Type 2 diabetes mellitus is made and the patient referred to an internist or endocrinologist for management.

Another unanswered question is who should manage such patients during pregnancy, as achieving tight glucose control is paramount. While trained obstetricians/gynecologists are educated in the management of gestational diabetes, it may be very difficult for the busy clinician to spend the extra time that each of these patients require. These women will commonly have weekly visits and frequent telephone contact. In addition, a host of other professionals such as dietitians, diabetic nurse educators, and skilled sonographers are required to provide optimal care. Any provider should not only be proficient in the management of patients with diabetes but also in women who are also pregnant with

Optimal Glycemic Control¹

	Pregnant
Fasting	65 - 100*
Pre-meal	60 - 105
Post meal	1 hr < 140 2 hr < 120
2 am - 6 am	65 - 135
HbA _{1c}	<6.0%

*mg/dl

Table 2: Optimal glycemic control for diabetes during pregnancy.

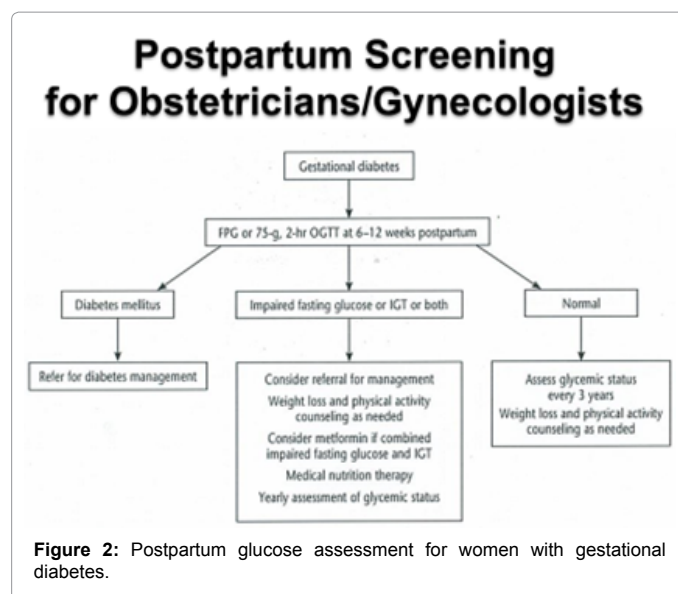


Figure 2: Postpartum glucose assessment for women with gestational diabetes.

disabilities. To have such resources within a busy practice as well as an obstetrician/gynecologist with the time to manage these patients may be overwhelming. Therefore, many obstetricians/gynecologists will team with an Internal Medicine physician or Endocrinologist who usually have access to diabetic centers (inside or outside of local hospital facilities) to establish cooperative management. Another method would be referral and subsequent co-management with Maternal-Fetal Medicine specialists. Finally, in complicated cases of gestational diabetes it may be optimal for the Maternal-Fetal Medicine specialist to primarily manage such women. For diabetic patients who live great distances from sub-specialist, telemedicine may be very helpful. It is important to remember that the goal of diagnosis and management of gestational diabetes is a healthy mother and a healthy baby not just during pregnancy and delivery but throughout life. By working together with the patients and physicians as well as other members of the health care team, we can achieve this goal.

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