

Obstetric Management in Gestational Diabetes

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Optimizing outcomes for women with gestational diabetes mellitus (GDM) and their fetuses requires not only careful metabolic management, but also appropriately applied fetal surveillance techniques and thoughtful selection of the most advantageous timing and route of delivery. Whenever possible, these clinical decisions should be based on the highest level of evidence available and should weigh the likelihood and seriousness of both maternal and fetal/neonatal morbidity. In areas where high-level evidence is lacking, resources should be channeled to designing and implementing clinical studies to get at good answers. In this review, we examine what new information exists in the area of obstetric care of women with GDM since the time of the Fourth International Workshop-Conference in 1997 and highlight areas where there remains a need for sound evidence on which to base practice guidelines.

The summary statement from the 1997 Workshop-Conference remarked that “the lack of data from controlled clinical studies on which management recommendations can be based was a prominent theme of discussion regarding antepartum management of GDM” (1). In the end, consensus was reached in the following areas of obstetric management:

Fetal surveillance:

- All women with GDM should monitor fetal movements during the last 8–10 weeks of pregnancy and report imme-

diately any reduction in the perception of fetal movements.

- Non-stress testing should be “considered” after 32 weeks’ gestation in women on insulin and “at or near” term in women requiring only dietary management.
- Biophysical profile testing and Doppler velocimetry to assess umbilical blood flow “may be considered” in cases of excessive or poor fetal growth, or when there are comorbid conditions, such as preeclampsia.
- Ultrasound should be used to detect fetal anomalies in women with GDM diagnosed in the first trimester or with fasting glucose levels >120 mg/dl.
- Amniocentesis to determine fetal lung maturity in preparation for delivery is not necessary in well-dated pregnancies after 38 weeks’ gestation.

Timing and route of delivery:

- The presence of GDM is not by itself an indication for cesarean delivery.
- GDM is not an indication for delivery before 38 weeks’ gestation in the absence of evidence of fetal compromise.

The consensus group lacked sufficient data to draw definitive conclusions on the following issues:

- The need for intensified fetal surveillance in women with GDM in good control on diet alone;
- The role of fetal weight estimation in

determining the timing and route of delivery;

- The optimal modality to predict the presence of fetal macrosomia and excessive/disproportionate fetal growth and the occurrence of shoulder dystocia and its resulting birth trauma.

ANTENATAL FETAL SURVEILLANCE

— Despite the lack of prospective data in this area, most authorities agree that women with GDM treated with insulin or glyburide, those in poor metabolic control regardless of treatment modality, and those with comorbid conditions (such as fetal growth abnormalities or hypertension) should undergo fetal surveillance in the form of non-stress testing, contraction stress testing, or biophysical profile assessments (1,2). Using treatment with insulin as a marker for increased fetal risk makes sense, given the fact that it is these women, not the ones easily controlled with diet, who are more likely to have unrecognized type 2 diabetes, a known risk factor for third trimester stillbirth (3).

It is unlikely that we will see a randomized trial specifically addressing the issue of whether or not women with diet-controlled GDM benefit from additional assessment of fetal well-being beyond daily fetal movement counts. The primary reason for this is that the outcomes of interest for such a trial (perinatal mortality and long-term neurological morbidities such as cerebral palsy) are relatively rare. For example, to detect a doubling of the stillbirth rate, an estimated sample size of 16,000 women was used (4).

If such evidence is absent, information might be drawn from existing and ongoing studies of GDM that include an unmonitored arm or cohort. In one small randomized trial looking at treatment and intensive monitoring versus no treatment and no formal fetal surveillance in women with GDM, no stillbirths occurred in the 150 women with GDM who had routine care and no antepartum fetal monitoring (5). Casey et al. (6) reported on various outcomes of 874 women with diet-controlled GDM compared with a large nondiabetic cohort. Women were classified as having diet-controlled GDM if their fasting glucose on the diagnostic 3-h

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Abbreviations: AD-BPD, abdominal diameter–biparietal diameter; EFW, estimated fetal weight; GDM, gestational diabetes mellitus; HAPO, Hyperglycemia and Adverse Pregnancy Outcome; MFMU, Maternal-Fetal Medicine Units Network.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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glucose tolerance test was <105 mg/dl. Fetal surveillance was not performed in these women unless another indication for doing so, such as preeclampsia, was found. Information regarding the proportion of the diabetic cohort who did undergo fetal surveillance was not provided. However, the perinatal mortality rate was identical between the two groups at 6/1,000, including comparable stillbirth rates (5/1,000 in the women with diet-controlled GDM and 4/1,000 in the nondiabetic women) (6). Notably, this cohort of women with diet-treated GDM may or may not have been “diet-controlled,” given the high rate of large-for-gestational-age and macrosomic infants (35 and 23%, respectively), but nonetheless experienced stillbirth rates comparable to a nondiabetic population without universal antenatal fetal surveillance. Thus, the severity of the disease process as evidenced by the glucose tolerance test results (i.e., the presence or absence of fasting hyperglycemia) may be a better indicator of fetal risk and the need for antepartum fetal testing than the treatment modality. Women with GDM who have fasting hyperglycemia are more likely to require insulin to control their glucose levels, but the decision to add such treatment is more subjective than the glucose tolerance test results.

Two large multicenter studies are currently underway to determine the impact of GDM on obstetric and perinatal outcomes: one conducted through the Maternal-Fetal Medicine Units Network (MFMU) of the National Institute for Child Health and Human Development (NICHD) and the multinational Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study. Both studies will provide prospective outcome data on a large number of women with GDM who do not receive treatment. The MFMU GDM trial will involve 950 women with abnormal glucose tolerance tests, but fasting glucose <95 mg/dl, randomized to treatment or routine care. These groups will be compared to a matched cohort of women with normal glucose screening results. Fetal surveillance in the form of non-stress tests will not occur in the treated group until 40 weeks' gestation, although women in either group may undergo fetal testing for other routine obstetric indications (7). Thus, this trial will give us information on almost 1,000 women with mild GDM who, by-and-large, will not be monitored with non-stress tests. If outcomes are better in the treated group than the untreated group

and comparable to a nondiabetic control cohort, but a relatively small proportion of them underwent fetal testing, it could be concluded that antenatal fetal testing does provide additional benefit to women with “mild” GDM (i.e., absence of fasting hyperglycemia). On the other hand, if treatment of mild GDM results in lower mortality and morbidity, but not to the level found in the nondiabetic women, it may be that fetal surveillance before 40 weeks has a place in identifying the pregnancies at highest risk and preventing adverse outcome.

The HAPO study is enrolling 25,000 women in 10 countries who will undergo 2-h 75-g glucose tolerance tests. As long as the fasting glucose level is <105 mg/dl and the 2-h postload value is below 200 mg/dl, the results of the glucose tolerance test will not be revealed to care providers, and all women in the cohort will be followed prospectively for various pregnancy outcomes. The sample size was planned to provide sufficient numbers across the spectrum of glucose values with the intent to identify thresholds useful for predicting morbidity attributable to GDM. For example, it is estimated that ~ 400 women in the cohort will have a fasting glucose value between 100 and 105 mg/dl (8). A large proportion of these women will not undergo treatment or tests of fetal well-being. Thus, the HAPO study, like the MFMU trial, will provide unprecedented data concerning the need for specialized fetal surveillance in pregnancies complicated by relatively mild glucose intolerance.

SHOULDER DYSTOCIA IN GDM: PITFALLS IN PREDICTION AND PREVENTION

— It is clear that women with GDM are at increased risk both for delivering an excessively grown infant and for having that delivery complicated by shoulder dystocia (9). When shoulder dystocia occurs, infants of mothers with diabetes are more likely to incur brachial plexus injury than infants of nondiabetic women (10–12). However, the best strategy for avoiding this outcome is a controversial topic, usually centered on the use of cesarean delivery to prevent difficult vaginal birth and thus injury to the infant. Although brachial plexus injury after cesarean delivery has been described (13,14), it is an exceedingly rare event (15). Unfortunately, few data currently exist to put an end to the controversy, which involves such emo-

tionally charged facets as devastating neonatal injury, avoidance of unnecessary maternal harm, and medicolegal liability. To compound the problem, the tools and methods we have at our disposal to predict the maternal-fetal pairs at highest or lowest risk of adverse outcome lack precision, while the personal and professional costs of making an incorrect clinical decision remain high. Although some progress has been made since the Fourth International Workshop-Conference in 1997, much work remains to be done.

At its core, this argument boils down to a diligent and thoughtful weighing of maternal and fetal risks: the chance of severe damage to the mother with GDM from cesarean delivery versus the chance of severe damage to her fetus from a shoulder dystocia event at vaginal delivery. Fortunately, both occurrences are relatively rare. The risk of brachial plexus injury (at least transient) when a macrosomic infant ($>4,000$ g) is delivered vaginally by a diabetic woman is ~ 2 –5% (10–12). Compiling data from several reports, Rouse and Owen (16) estimated that the mean probability that a brachial plexus injury will persist is 6.7%. Therefore, out of 10,000 vaginal deliveries of macrosomic infants, ~ 13 –33 will result in persistent brachial plexus injury, of which roughly three-quarters can expect full recovery of shoulder and elbow function when surgery is performed in the first year of life (17). Even with complete brachial plexus palsy, involving the hand and associated with Horner's syndrome, staged surgical intervention over the first 3–4 years of life can provide useful hand function in 76% of cases (18). Nonetheless, avoidance of such an outcome in the first place is preferable, leading us to consider the maternal burden of morbidity from elective prelabor cesarean delivery.

It is widely assumed that cesarean delivery results in more maternal morbidity and, indeed, mortality than vaginal delivery, and some evidence exists for a two- to fourfold greater risk of maternal death in women delivered by cesarean delivery compared with vaginal delivery (19). However, women with complications that increase the risk of maternal death and serious morbidity, such as severe hypertensive disease, hemorrhage from placenta previa or abruption, true obstructed labor, and life-threatening infections, often are delivered by cesarean section, making it difficult to discern the risk attributable to the operative intervention itself. Conversely, it is difficult to find data

indicating that an elective prelabor cesarean delivery at term is any riskier than vaginal delivery. Information from the Washington state birth events records database from 1990 indicates that women delivering a macrosomic infant by prelabor cesarean section have a threefold greater risk of postpartum infection, an 11-fold greater risk of wound complications, but an 80% lower risk of postpartum hemorrhage than women experiencing a vaginal delivery of a macrosomic infant. Overall, rates of each complication were low in both groups (15). However, the cumulative risk of repeated cesarean deliveries needs also to be considered and factored into clinical decision making. Besides the well-known risks to the mother of placenta previa/accreta with a uterine scar (20), newer data indicate that prior cesarean delivery increases the risk for stillbirth in subsequent pregnancies (21).

Thus, it appears that avoiding vaginal delivery benefits the infant destined to suffer shoulder dystocia and brachial plexus injury, whereas elective prelabor cesarean delivery poses relatively minor risk to mothers. The key, then, is to accurately identify the maternal-fetal pairs who need such intervention and allow the others to labor. However, we currently lack the capability to do so with acceptable precision. The problem is that identifying the large fetus is not enough. We really want to identify the fetus whose excessive disproportionate growth will result in its negotiating the birth canal to a sufficient degree to prevent arrested labor, but who will then experience a shoulder dystocia. Once a shoulder dystocia occurs, its recognition and management may affect the likelihood of brachial plexus injury. On the other hand, there may be something we don't understand about the interaction between the maternal pelvis and soft tissues and the fetus that makes a shoulder dystocia more difficult to relieve, thus placing the infant at increased risk for injury despite our most careful maneuvers. We currently lack the ability to get at these complex interactions in a clinically useful way.

However, the well-intentioned desire to avoid birth trauma remains, and thus we attempt to antenatally detect the large fetus, who is more likely to suffer a shoulder dystocia and nerve injury (9,11). The two most widely available means of estimating fetal weight, clinical assessment and ultrasound, have been shown to have

roughly equivalent accuracy, even in macrosomic fetuses (22–24), making it difficult to recommend one method over the other based on hard evidence. Nonetheless, obtaining a fetal weight estimate by ultrasound provides some measure of objectivity over clinical estimation and has been shown to be as accurate in obese women as in lean women (25).

Some evidence exists that using ultrasound-derived fetal weight estimates to inform decisions regarding timing and route of delivery in diabetic women can result in lowered rates of shoulder dystocia. We published our experience with a clinical policy of obtaining an ultrasonic estimated fetal weight (EFW) at 37–38 weeks in women with diabetes who were eligible for vaginal delivery and used the results as follows: when the EFW was >4,250 g, cesarean delivery was recommended, and when the EFW was above the 90th percentile (and below 4,250 g), labor induction was performed. We compared the shoulder dystocia rates among 1,337 women managed under this protocol to a historical cohort of 1,227 women managed without; antenatal management of diabetes was otherwise similar between the two time periods. The shoulder dystocia rate in the cohort in whom the EFW protocol was used was significantly decreased in the overall diabetic population: 1.5 vs. 2.4% (OR 0.5, 95% CI 0.3–1.0). The largest impact was found in the fetuses at greatest risk: the shoulder dystocia rate among macrosomic infants was 19% before the EFW protocol and 7% using the protocol (OR 0.3, 95% CI 0.1–1.0). The EFW protocol affected the timing and route of delivery of only 10.6% of our diabetic population (6.8% labor induction and 3.8% cesarean delivery), which compares favorably to the 9% rate of macrosomia that was found in this cohort. Despite this relatively low rate of intervention, the protocol probably resulted in a significant increase in our overall cesarean delivery rate among diabetic women after its implementation (25.1%, up from 21.7% in the earlier time period) (26). These data also have the advantage of being derived from a single center's population, pointing out the important, but poorly studied, impact of local practice styles, baseline macrosomia and cesarean delivery rates, and patient population characteristics on the cost-benefit balance of cesarean delivery to prevent brachial plexus injury.

Little additional information regarding the timing of delivery in women with

GDM has emerged since the Fourth International Workshop-Conference. Yogev et al. (27) reported their experience with a clinical protocol in which 84 women with GDM underwent labor induction at 38–39 weeks if they were treated with insulin and/or the fetus was above the 90th percentile (but below 4,000 g) by ultrasound estimation. The overall cesarean delivery rate in this cohort was 18%, significantly higher than in a cohort of nondiabetic women in spontaneous labor (9%), but no different than in a group of nondiabetic women who underwent elective labor induction (14.8%). This clinical policy resulted in a macrosomia rate of only 5.7% in this group of women. No comparison to a similar population managed without this protocol is provided, and therefore the impact of this practice on outcomes cannot be determined. Shoulder dystocia rate is also not reported.

How might we refine and improve our approach to selecting the maternal-fetal pairs that would most benefit from avoiding vaginal delivery? More accurate estimation of fetal weight/prediction of birth weight would minimize maternal morbidity from cesarean sections done in error for suspected macrosomia. Alternatively, being able to accurately detect the fetal body asymmetry and/or the fetal-pelvic disproportion that might contribute to shoulder dystocia (and perhaps brachial plexus injury) risk would be helpful. Currently, however, little data exist along these lines. Magnetic resonance imaging and three-dimensional ultrasound are promising new modalities that may improve fetal weight estimation by providing volumetric assessments of the fetus. Results from various reports are summarized in Table 1. In general, both three-dimensional ultrasound and magnetic resonance imaging result in more accurate fetal weight estimates than two-dimensional ultrasound. Most of these studies are limited in their applicability to the issue of fetal weight estimation in diabetic women for several reasons: overall sample sizes are small, few include or have much less focus on a diabetic population, and fetuses at the extremes of weight are few in number. In addition, the performance of these modalities in routine clinical use (i.e., outside of a research setting) has not been evaluated, and their availability and cost are also potential obstacles.

Although a great deal of work has been done to sonographically identify the

Table 1—Summary of studies of volumetric assessment of fetal weight

Author	Imaging modality	n	Include diabetic women?	Findings	Comments
Uotila et al. (30)	MRI	20	Yes, 10 type 1 diabetes	MRI (10-mm sagittal slices) more accurate than 2D US at predicting BW	“Most” fetuses were LGA; imaging completed in under 1 min
Schild et al. (31)	3D US	125 + 65	Unknown	3D US formula (thigh volume, upper arm volume, abdominal volume, BPD) more accurate than 2D US at predicting BW	13 macrosomic infants, 22 LGA infants
Tukeva et al. (32)	MRI	8	Yes, all	MRI measurement (TrueFISP) of fetal shoulder width was closely correlated with actual shoulder width	All had suspected macrosomia; 7/8 were delivered by cesarean section
Hassibi et al. (33)	MRI	35	Unknown	MRI (8-mm axial images) significantly better than 2D US (Hadlock) at predicting BW	Imaging time was 90 s
Lee et al. (34)	3D US	100	Unknown	3D US (fractional thigh volume + AC) significantly better than 2D US at predicting BW	

2D, two-dimensional; 3D, three-dimensional; AC, abdominal circumference; BPD, biparietal diameter; BW, birth weight; LGA, large-for-gestational-age; MRI, magnetic resonance imaging; TrueFISP, true fast imaging with steady-state precession; US, ultrasound.

“fat” fetus, with varying degrees of success, most studies have reported the accuracy of predicting birth of a large infant, rather than correlating these findings to obstetric outcomes such as shoulder dystocia or labor abnormalities. Cohen et al. (28) describe the use of the abdominal diameter–biparietal diameter (AD-BPD) difference to identify a pregnancy at risk for shoulder dystocia. In a group of 31 women with diabetes, all of whom were suspected of carrying a large fetus, they found no difference in maternal characteristics or birth weight between the deliveries complicated by severe shoulder dystocia and those with uncomplicated vaginal delivery. However, the mean AD-BPD difference was higher in the shoulder dystocia group (3.1 vs. 2.6, $P = 0.05$). The cutoff of 2.6 resulted in 100% sensitivity (all cases of shoulder dystocia were above this cutoff) and 46% specificity. The authors describe a 30% positive predictive value in predicting severe shoulder dystocia for an AD-BPD difference of at least 2.6, but this number is almost certainly an overestimate, given the fact that their cohort included only vaginal deliveries. It is likely that a substantial proportion of large fetuses with an AD-BPD difference above this threshold will undergo cesarean deliveries for labor abnormalities; inclusion of these cases in the denominator of the positive predictive value calculation would lower that num-

ber. In another study, a cohort of 84 women with infant birth weight $>4,000$ g was compared with 84 women delivering nonmacrosomic infants. Of the 65 vaginal deliveries in the macrosomic group, 13% were complicated by shoulder dystocia. The authors found that an abdominal circumference of at least 35 cm, obtained within 2 weeks of delivery, had a sensitivity of 93% and specificity of 88% for macrosomia (29). They describe positive and negative predictive values that appeared good, but were invalid because of the case-control design of the study. Thus, we are again left with sonographic findings with good sensitivity, but unknown (and likely poor) positive predictive value, the component of test accuracy that would be most helpful in identifying before delivery those at highest risk for difficult birth.

To help resolve this issue of the value of sonographic or magnetic resonance imaging detection of the excessively grown fetus, we require studies with the following characteristics: a large cohort of diabetic women; imaging obtained within a short time frame before delivery and in all women regardless of clinical estimate of fetal size; comprehensive ultrasound measurements, including specialized measures such as shoulder soft tissue thickness and cheek-to-cheek diameter, in all women; and a reasonably high rate of vaginal delivery from which we may begin to identify better markers for, if not

brachial plexus injury, at least shoulder dystocia.

SUMMARY — Reviewing the areas of controversy related to the obstetric management of women with GDM, we are unfortunately unable to provide significant refinement of the recommendations agreed upon after the Fourth International Workshop-Conference due to the lack of properly controlled and powered clinical studies in this area since 1997. In the area of the need for antenatal fetal surveillance in women with milder degrees of GDM, we may be able to draw indirect conclusions from ongoing cohort studies that will include large numbers of women. In the area of optimal timing and mode of delivery to avoid fetal injury, large well-controlled prospective studies do not currently exist and are urgently needed. In addition, refinement of fetal and pelvic imaging techniques to more accurately identify the maternal-fetal pairs most likely to benefit from avoiding vaginal delivery, and the more widespread availability of these technologies, may also prove to be of benefit in the obstetric management of women with GDM.

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