

# Fetal Weight Estimation in Diabetic Pregnancies and Suspected Fetal Macrosomia: The Real Facts

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**P**regnancy is often complicated by diabetes, either preexisting or diagnosed during gestation. The reported prevalence of gestational diabetes mellitus (GDM) is 3% to 5% of all live births [1], and even higher in selected populations, such as Mexican-Americans, Asians, and Indians [2,3]. Clinicians have witnessed a significant improvement in outcome of diabetic pregnancies owing to improved perinatal maternal glycemic control, close antepartum surveillance, and advances in neonatal care, although the risk of fetal macrosomia and adverse perinatal outcome has not been eliminated.

Ultrasound is an important tool for monitoring diabetic pregnancies. It is used to assess gestational age, congenital anomalies, fetal well-being (dynamic assessment), and growth abnormalities such as macrosomia and fetal growth restriction. However, the role of fetal weight estimation by ultrasound in predicting adverse perinatal outcome remains controversial. The failure to correctly estimate fetal weight has important clinical implications and has been incorporated in litigations involving complicated deliveries, which in rare cases can result in persistent brachial plexus injury.

This paper reviews the literature on the accuracy of ultrasound in estimating fetal weight in diabetic pregnancies. We focused specifically on its role in the prediction and clinical management of fetal macrosomia.

## Macrosomia

Excessive fetal growth is defined in two ways. Infants large for gestational age (LGA) have a birth weight equal to or greater than the 90th percentile for their gestational age. This factor, however, varies according to the specific population under study. In the United States, for example, a recent national survey reported that fetal weight in the 90th percentile at 37, 40, and 42 weeks of gestation is 3,755, 4,060, and 4,098 gr, respectively [4]. Fetal macrosomia is defined as growth beyond a specific weight, usually 4,000 or 4,500 gr, regardless of gestational age. The risk of morbidity in infants and mothers when the birth weight is between 4,000 and 4,500 gr is greater than that in the general obstetric population, and it increases sharply beyond 4,500 gr. This cutoff is supported by recent large cohort studies [5].

Ten percent of all live-born infants in the United States weigh more than 4,000 gr, and 1.5% weigh more than 4,500 gr [1]. Both gestational and pregestational diabetes are associated with fetal macrosomia. In one study, 6% of mothers with untreated borderline GDM delivered infants weighing more than 4,500 gr, compared with only 2% of women with normal glucose tolerance [6]. If full-blown GDM is unrecognized and untreated, the risk of macrosomia may be as high as 20% [7].

## Shoulder dystocia

Shoulder dystocia is the most serious complication of fetal macrosomia; the risk is 1.4% for all vaginal deliveries [8], and it rises dramatically to 9.2% - 24% when the birth weight exceeds 4,500 gr [9, 10]. In diabetic pregnancies, birth weights greater than 4,500 gr have been associated with 19.9% to

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50% rates of shoulder dystocia [9, 10]. Shoulder dystocia may also be associated with other birth traumas, such as Erb's palsy, clavicular fracture, fetal distress, low Apgar score, and birth asphyxia [11], although 25 to 75% of brachial plexus injuries are unrelated to antecedent shoulder dystocia [12].

Macrosomia due to maternal diabetes is different from macrosomia due to other predisposing factors [13, 14]. Macrosomic infants of diabetic mothers tend to have greater total body fat, greater shoulder and upper-extremity circumferences, greater upper-extremity skin-fold measurements, and smaller head-to-abdominal-circumference ratios than macrosomic infants of nondiabetic mothers. This may explain the higher incidence of shoulder dystocia in these infants [14].

Ideally, clinicians should diagnose macrosomia in the antenatal period so that they can offer the optimal mode of delivery for preventing shoulder dystocia on the one hand, and sparing unnecessary cesarean sections on the other.

#### **Ultrasonographic diagnosis of fetal macrosomia**

The diagnosis of fetal macrosomia has been the subject of much clinical concern and scientific investigation. Over the past 30 years, investigators have introduced formulas based on sonographic measurements of fetal organs to estimate fetal weight. The older formulas used the fetal head, abdomen, and femur, either alone [15] or in combination [16, 17]. Some authors demonstrated differences in accuracy and precision among these formulas [18, 19]. Regardless of the formula used, the accuracy of the fetal weight estimation decreased with increasing birth weight [20-22]. For example, Hadlock's formula has a mean absolute percent error of 13% for infants weighing more than 4,500 gr but only 8% for nonmacrosomic infants [23]. Others showed that in women without diabetes, ultrasound biometry used to detect macrosomia has a sensitivity of 22-44%, specificity of 99%, positive predictive value of 30-44%, and negative predictive value of 97-99% [18, 24]. In addition, the error rates of the regression functions that generate the sonographic estimates of fetal weight are similar to the error rates of the clinical estimates [25]. Ultrasonographic fetal weight estimation at the 90th percentile or above has a sensitivity range of 6.7-89%, and a specificity range of 62-98%. The same calculation for birth weight of 4,000 gr or more has a sensitivity range of 11-100% and a specificity range of 48-100% [25]. O'Reilly-Green and Divon [24] and Miller et al. [26] found that the optimal cutoff

for sonographic fetal weight estimation in predicting a birth weight of  $\geq 4,000$  gr is 3,700 gr. The prediction of macrosomia in fetuses in breech presentation is more difficult than in fetuses in cephalic presentation [27]. The reported mean absolute percent error for breech and cephalic presentations are 12.9% and 9.5%, respectively.

To overcome these drawbacks, alternative sonographic markers for fetal macrosomia have been proposed which take advantage of the presumed correlation between subcutaneous fat deposition and fetal weight. Three-dimensional ultrasound measurements of fetal upper arm volume [28, 29], fetal chest [30], abdominal [31] and humeral [32] soft tissue thickness, and cheek-to-cheek diameter [33], as well as of the subcutaneous tissue/femur length ratio [34, 35], are associated with varying efficacies. Sacks and Chen [36] reviewed population-based studies of the clinical performance of ultrasound in predicting macrosomia. They concluded that only 15 to 81% of babies (median 67%) predicted to be macrosomic are indeed macrosomic at birth, and that 50 to 100% (median 62%) of all cases of macrosomia are successfully predicted by sonographic measurements. Therefore, like with clinical estimates of fetal weight, the true value of ultrasonography in the management of fetal macrosomia may be its ability to rule out the diagnosis (negative predictive value) [5]. This is especially important given the fact that clinicians who suspected fetal macrosomia on the basis of an ultrasound were more likely to diagnose labor abnormalities and were more likely to perform cesarean deliveries despite normal birth weights [37].

Individualized fetal growth estimation curves, such as the complex mathematical model of Rossavik, have not proven more accurate. The prediction error of Rossavik's model averaged 6.1% and ranged from 3.6% to 16.5% [25]. By contrast, serial measurement of the abdominal circumference (AC) had a sensitivity and specificity of 84% and 100%, respectively, in predicting birth weight in the 90th percentile or above [38]. For single measurement the sensitivity and specificity were 54% and 89%, respectively. A single measurement of abdominal circumference above the 90th percentile has a relative risk of only 5.5 for birth weight in the 90th percentile or above, whereas serial measurements have a relative risk of 32 [25].

Other techniques for estimating fetal weight have been reported as well, such as magnetic resonance imaging, which yielded estimates within 3% of the actual birth weight in 11 patients with babies weighing 1,600 – 3,300 gr. This compared favorably

rably with the 6.5% error by sonographic examination of the same patients [39].

#### **Prediction of macrosomia in diabetic pregnancies**

The estimation of fetal weight in diabetic pregnancies involves special considerations. Because of the disproportionate contribution of fat to fetal body weight and the lower density of fat compared to lean body tissue, equations derived from cross-sectional data may theoretically overestimate the fetal weight when applied to the GDM population [40]. Furthermore, the time from examination to delivery may influence the accuracy and precision of the sonographic estimates [24, 41, 42].

Currently, no single sonographic measurement is capable of distinguishing between LGA and appropriate-for gestational-age (AGA) infants in diabetic pregnancies. Although the finding of an abdominal circumference above the 90th percentile in the second or third trimester is positively associated with fetal macrosomia, the actual birth weights of the babies predicted to be macrosomic on this basis overlap with those of AGA babies in a substantial proportion of cases [43].

Clinical studies have found no significant differences in absolute percent error of birth weight between infants of women with and without diabetes [23]. The accuracy of birth weight prediction by ultrasound and by clinical estimates has been analyzed in a number of studies [44-49]. When the sample was limited to babies with an actual birth weight of >4,000 gr, no significant differences were found between the clinical and ultrasound estimates at or near the onset of labor. The sensitivity of the sonographic estimates in predicting birth weight at the 90th percentile or above in diabetic pregnancies ranged from 70-96%, and specificity ranged from 77-100% [25]. Corresponding values for predicting a birth weight of  $\geq 4,000$  gr were 33-69% and 77-98%.

Other measurements did not prove superior in diabetic pregnancies [25]. These included the femur length/ abdominal circumference ratio, the abdominal diameter/ femur length ratio, the chest/ biparietal diameter ratio, and soft tissue thickness. Cohen et al [50], in a study of the value of the difference between the abdominal and biparietal diameters in predicting shoulder dystocia in diabetic pregnancies, found that the cutoff value of  $\geq 2.6$  cm had a sensitivity of 100% and a specificity of 56%.

Hendrix et al [51] reported that when birth weight was 4,000 gr or more, the absolute error of the clinical estimates was 5.3% and of the sonographic

estimates, 13%. Ninety-two percent of the clinical estimates were within 10% of the birth weight compared with 33% of the sonographic estimates. McLaren et al. [52] showed that the 90% prediction limits for an estimated fetal weight of 4,000 gr in diabetic pregnancies included birth weights from 3,410 to 4,675 gr. When the birth weight exceeded 4,500 gr, only 50% of the fetuses actually weighed within 10% of the ultrasound-derived estimate [53].

#### **Role of ultrasound in the management of diabetic pregnancy**

Glucose intolerance and fetal abdominal circumference

Parretti et al. [54] recently showed that fetal abdominal circumference, which is considered as a parameter of growth of insulin-sensitive tissues, is influenced by postprandial glucose peaks even in nondiabetic pregnancies. They examined the correlations between maternal glucose levels and sonographic parameters of fetal growth in a longitudinal study of 51 Caucasian nonobese pregnant women with normal glucose challenge tests. Results showed that concomitant with a slight but progressive increase in daily mean glucose levels from 28 weeks ( $71.9 \pm 5.7$  mg/dl) to 38 weeks ( $78.3 \pm 5.4$  mg/dl), demonstrating the known deterioration of glucose tolerance during the course of normal pregnancy, there was a significant positive correlation at 28 and 36 weeks of gestation between postprandial glucose values and fetal abdominal circumference, and a negative correlation between head-abdominal circumference ratio and 1-h postprandial blood glucose values.

These findings are in agreement with those of diabetic pregnancies, in which a 1-h postprandial maternal blood glucose concentration in the third trimester is considered a strong predictor of infant birth weight and fetal macrosomia [55]. Furthermore, in diabetic pregnancies, fetal hyperinsulinism and birth weight have been found to correlate best with 1-h postprandial glucose values [56]

#### **Insulin treatment**

Buchanan et al. [57] suggested that insulin may treat early macrosomia diagnosed in ultrasound. They randomized 98 women at 29-33 weeks' gestation with a fetal abdominal circumference exceeding the 75th percentile for gestational age to either diet therapy alone or diet therapy with twice-daily insulin. They found that the addition of insulin decreased the likelihood of birth weight greater than the 90th percentile from 45% among those treated with diet only to 13% among those rece-

iving insulin.

Recently, the same group of investigators [58] compared management based on maternal glyce-mic criteria with management based also on fetal abdominal circumference measurements in order to select patients for insulin treatment of GDM. Ninety-eight women with GDM and fasting hyperglycemia were randomized to two groups: insulin treatment or insulin treatment only if abdominal circumference was at the 70th percentile or greater and/or if any venous fasting plasma glucose measurement was >120 mg/dl. The authors found no between-group differences in birth weight, frequency of birth weight above the 90th percentile (6.3% vs 8.3%), or neonatal morbidity. Thus, in women with GDM and fasting hyperglycemia, measurements of glucose plus fetal abdominal circumference identified pregnancies at low risk of macrosomia and sparing in 38% of the patients of insulin therapy with no increase in neonatal morbidity.

#### **Fetal weight estimation and prophylactic cesarean delivery**

Macrosomia is distinctly more common in women with GDM, and shoulder dystocia is more likely at a given birth weight in pregnancies complicated by diabetes than in nondiabetic pregnancies. Therefore, it may be reasonable, to recommend cesarean delivery without a trial of labor at some particular threshold of fetal weight. However, the clinical effectiveness of this practice has not yet been established [5]. According to one observational study in which 1,337 women with diabetes were offered either elective cesarean delivery if the ultrasound-derived fetal weight estimate was beyond 4,250 gr or induction of labor if the ultrasound predicted an LGA infant but weighing less than 4,250 gr [59]. Findings were compared with a historic control group of 1,227 women with diabetes. Results yielded a nonsignificant reduction in the risk of shoulder dystocia from 2.4% in controls to 1.1% in the intervention group, and a significant increase in cesarean delivery rate from 21.7% in controls to 25.1% in the intervention group.

In two additional reports analyzing the policy of prophylactic cesarean delivery for macrosomia, which took into account the reported sensitivity and specificity of ultrasonography, the authors calculated that 3,695 cesarean deliveries would be required to prevent one permanent injury, at a cost of \$8.7 million for each injury avoided [60,61]. For pregnancies complicated by diabetes, these figures were still high at 443 cesarean deliveries to prevent a single permanent injury.

On the basis of these findings, the American College of Obstetricians and Gynecologists [5] stated that, "Because of the lack of well-designed and well-executed randomized clinical trials, a policy of prophylactic cesarean delivery for suspected fetal macrosomia less than 5,000 g may not be effective for pregnancies without diabetes. Furthermore, even for pregnancies complicated by diabetes, the cost-effectiveness of such a policy is doubtful." They concluded that, "Although the diagnosis of fetal macrosomia is imprecise, prophylactic cesarean delivery may be considered for suspected fetal macrosomia with estimated fetal weights greater than 5,000 g in women without diabetes and greater than 4,500 g in women with diabetes". However, these conclusions were modified in their latest Practice Bulletin [62], which suggested that, "Because of the higher likelihood of shoulder dystocia at a given birth weight in the pregnancies of women with diabetes, it may be best to apply the above recommendation to an estimated fetal weight greater than 4,000 g for GDM. Operative deliveries from the midpelvis should be avoided, if possible, in patients with GDM who have an estimated fetal weight of 4,000 g or more and a prolonged second stage of labor "

#### **Summary**

Ultrasound is a useful predictor of macrosomia from a statistical point of view [25], but it has limited applications in clinical practice because of its substantial false-positive and false-negative rates [25]. Serial sonographic measurements can increase the positive predictive value. One study suggested that sonographic laboratories might improve their results by performing receiver operator characteristics (ROC) curve analysis on their own data, in order to select a better cutoff value to predict macrosomia [25].

On the basis of the data collected so far, several key statements can be made regarding the accuracy of ultrasound in predicting fetal macrosomia:

1. Regardless of the formula used, the accuracy of the EFW decreases with increasing birth weight.
2. A disparity in ultrasound measurements between by different operators in individual subjects should be taken into account.
3. Formulas incorporating measurements of the fetal head are of less clinical value for patients in labor.

4. The time elapsed between the fetal weight estimation and delivery may influence the accuracy and precision of the estimate.
5. Although variations in either maternal obesity or amniotic fluid index alone do not significantly influence predictive accuracy, the combination of maternal obesity, anterior placentation and oligohydramnios may eliminate the possibility of accurately measuring fetal parts.
6. The diagnosis of fetal macrosomia is imprecise. For suspected fetal macrosomia, the EFW using ultrasound biometry is believed to be no more accurate than the EFW obtained by clinical palpation [5, 49]. However, a recent prospective study showed that the accuracy of ultrasound estimation of fetal weight was better than maternal and clinical estimation of fetal weight [63].
7. To date, non of the management algorithms developed for selective interventions that are based on the sonographic EFW have demonstrated any efficacy in reducing the incidence of either shoulder dystocia or brachial plexus injury.

Should ultrasound be used to identify fetal macrosomia in low-risk pregnancies or in pregnancies complicated by diabetes? It is clear that ultrasound-derived fetal weight estimates alone are not sufficient grounds for deciding the route of delivery [5, 64]. To assess the risk of macrosomia in both diabetic and nondiabetic pregnancies, other known risk factors should also be taken into account, such as prior history of macrosomia, maternal pre-pregnancy weight, weight gain during pregnancy, multiparity, fetal sex (male), gestational age (>40 weeks), ethnicity, maternal birth weight, and maternal height [5]. To determine the mode of delivery, the clinical fetal weight estimate, subjective maternal weight estimate, and clinical pelvimetry findings should be added to the sonographic fetal weight estimate (preferably by serial measurements which include the abdominal circumference), with consideration of the above risk factors for macrosomia. Furthermore, as suggested recently [65], the use of additional examiners to perform the sonographic estimates may reduce the absolute weight difference, especially with repeated measurements of abdominal circumference.

In the future, three-dimensional ultrasound and magnetic resonance imaging are expected to gene-

rate better ROC curves than those of two-dimensional ultrasound or clinical estimates [25].

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