Accuracy of Third Trimester Ultrasound for Predicting Large-for-Gestational Age Newborn in Women with Gestational Diabetes Mellitus

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ABSTRACT

Objective: To determine the accuracy of ultrasonography during 32-36 weeks of gestation for predicting a large-for-gestational-age (LGA) newborn in women with gestational diabetes mellitus (GDM).

Materials and Methods: Women with singleton pregnancy, aged ≥ 18 years old and diagnosed with GDM were recruited. They underwent ultrasonography at 32-36 weeks' gestation for fetal biometry, namely, biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), and femur length (FL). Estimated fetal weight (EFW) was derived from these 4 parameters by Hadlock formula. Delivery of an LGA newborn in women with the ultrasound finding of LGA fetus was the primary outcome of interest along with determination of predicting factors.

Results: Of 345 studied women, 107 (31%) had an LGA newborn. EFW of ≥ 90th percentile at third trimester ultrasonography was found in 13 women, all of whom had an LGA newborn. It had a positive predictive value (PPV), specificity, sensitivity and negative predictive value (NPV) of 100%, 100%, 12.1% and 71.7% respectively to predict LGA at birth. Considering each fetal parameter individually, AC ≥ 90th percentile and HC ≥ 90th percentile had odds ratios (OR) with 95% confidence intervals of the newborn being LGA of 6.5 (3.3-12.8) and 2.0 (1.0-4.0) respectively while EFW ≥ 85th percentile had the highest OR of 9.3 (1.1-77.9). Lowering cutoff values of EFW to 80th and 70th percentile increased the sensitivity and NPV for prediction of LGA at birth while reducing the PPV and specificity slightly.

Conclusion: EFW derived from the third trimester ultrasonography in women with GDM had high PPV and specificity with low to moderate sensitivity and NPV to predict an LGA newborn in women with GDM.

Keywords: Estimated fetal weight; third trimester ultrasound; large-for-gestational age newborn; gestational diabetes mellitus (Siriraj Med J 2021; 73: 322-329)

INTRODUCTION

Gestational diabetes mellitus (GDM) is a condition diagnosed during pregnancy associated with a lack of tolerance to increased blood glucose level.[1] Approximately 7% of all pregnancies are affected, with a worldwide incidence of more than 200,000 pregnancies annually.[2] During the past decade, the incidence of GDM in Siriraj Hospital, a Thailand national tertiary center, has increased from 2-3% to 10-15%.

GDM can cause adverse maternal and fetal/neonatal outcomes such as the need for cesarean delivery, cephalopelvic disproportion, postpartum hemorrhage,

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pregnancy-induced hypertension, large-for-gestational age (LGA) fetus, shoulder dystocia, neonatal hypoglycemia, and jaundice.[3,4] The incidence of LGA fetus in women with GDM was reported in the range of 15-20%.[3,5,6] The ability to diagnose LGA fetus in GDM women in advance would improve the management and outcomes of both women and their babies.

Ultrasonography in the third trimester was proven to be useful for predicting the actual birth weight.[7,8] Ultrasonography has been reported to help guide management and improve pregnancy outcomes in women with GDM.[9] However, to our knowledge, no study has addressed the accuracy of the third trimester ultrasound at 32-36 weeks' gestation, which is the period just after the maximal fetal growth rate, for predicting an LGA newborn in these women.

The current study was performed to determine the accuracy of ultrasound during 32-36 weeks' gestation for predicting LGA newborn in women with GDM.

MATERIALS AND METHODS

This prospective cohort study was performed at Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand during January 2017 to January 2018. Women aged ≥ 18 years with a singleton pregnancy at 32-36 weeks' gestation, diagnosed with GDM, and without known fetal anomalies were included. The study was approved by the Siriraj Institutional Review Board (SIRB) (Si 007/2017). Written informed consent was obtained from all women.

Gestational age was based on either crown-rump length in the first trimester or last menstrual period correlating with BPD in the second trimester. Screening for GDM with 50-g glucose challenge test (50-g GCT) was performed in pregnant women with any of the following risk factors: age ≥ 30 years old, BMI >25 kg/m^2, family history of diabetes mellitus, history of GDM in previous pregnancy, history of dead fetus in utero (DFIU), fetal anomaly or a macrosomic baby in a previous pregnancy[10]. Women with an abnormal 50-g GCT (≥ 140 mg/dl) underwent a 100-g oral glucose tolerance test (OGTT). According to Carpenter-Coustan criteria, GDM was diagnosed when two or more values were abnormal.

The women underwent ultrasound scanning using a machine with a 2-5 MHz curvilinear transabdominal transducer (Voluson E8; GE Healthcare, Zipf, Austria). Fetal biometry, namely, biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), and femur length (FL), were measured by an experienced physician. With inappropriate fetal position or acoustic shadows, remeasurement was performed after a short break until standard planes were achieved in all pregnant women. Three measurements were obtained for each parameter and the averages were used to calculate the estimated fetal weight (EFW) by Hadlock formula.[10] EFW percentile was determined and was classified as small-for-gestational age (SGA) if the EFW was ≤ 10th percentile, LGA if the EFW was ≥ 90th percentile, and appropriate-for-gestational age (AGA) if the EFW was in the range between these two limits. Birth weight was classified as LGA (≥ 90th percentile) or SGA (≤ 10th percentile) status based on 2004-2008 WHO Global Survey on Maternal and Perinatal Health (WHOGS) data.[12] Macrosomia was defined when birth weight was 4,000 grams or more.

Body mass index (BMI) was categorized into four groups according to the 2009 Institute of Medicine (IOM)/National Research Council (NRC) guidelines as follows: underweight (BMI < 18.5 kg/m^2), normal (BMI 18.5-24.9 kg/m^2), overweight (BMI ≥ 25.0-29.9 kg/m^2), and obese (BMI ≥ 30.0 kg/m^2). Recommended total weight gain in each group is 13-18 kg, 11-16 kg, 7-11 kg, and 5-9 kg, respectively.[13] Overweight and obese groups were defined as high BMI.

GDM management started wth proper exercise and diet adjustment. Insulin would be added in cases uncontrollable by these two strategies. Glycemic follow-up checks were performed using either fasting blood sugar (FBS) (normal value: < 95 mg/dl) with two-hour postprandial (2-h PP) blood sugar (normal value: < 120 mg/dl) or 2-h PP alone. GDM diagnosed before 24 weeks of gestation was defined as early GDM, and GDM diagnosed after 24 weeks was defined as late GDM.[11]

Maternal complications, including gestational hypertension, preeclampsia, shoulder dystocia, 3rd or 4th degree laceration of birth canal, postpartum hemorrhage, and preterm delivery were recorded. Neonatal outcomes, including birth weight, birth asphyxia, subgaleal hematoma, hypoglycemia, polycythemia, jaundice, respiratory distress syndrome, and NICU admission, were also studied.

Statistical analysis

SPSS Statistics version 21 (SPSS, Inc., Chicago, IL, USA) was used for statistical analyses. Sample size was calculated based on the study of Scifres et al.[14], showing that the accuracy of third trimester ultrasound was 22.6% for predicting LGA newborn in women with GDM. With the error of 30% and loss of data of 10%, the required total sample size was 360.

Demographic data were summarized using descriptive statistics. Data are presented as number and percentage

for categorical variables, and mean ± standard deviation for continuous variables. Student's t-test or Chi-square test was used to compare patient data between groups. Results of multivariate analysis are shown as adjusted odds ratio and 95% confidence interval. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and cut-off value of third trimester ultrasound for predicting LGA newborn in women with GDM were also calculated. P-value of < 0.05 was considered statistically significant.

RESULTS

Of the 360 pregnant women initially recruited, 15 women were lost to follow-up and 345 women were included in the final analysis. The demographic and clinical characteristics of the women are shown in Table 1. Forty percent of the women had a high BMI. Almost two-thirds of women were diagnosed with GDM before 24 weeks' gestation. Approximately 90% of women did not need insulin therapy. The three most common risk factors for GDM were age ≥ 30 years old, BMI > 25 kg/m^2 and family history of diabetes mellitus.

Fetal parameters at 32-36 weeks' gestation are shown in Table 2. BPD, HC and FL of ≥ 90th percentile each accounted for 35.9-38.0% of women, and 20.3% of women had AC of ≥ 90th percentile. EFW of ≥ 90 percentile (LGA) was present in 13 (3.8%) fetuses.

Maternal and neonatal outcomes are described in Table 3. Forty-two percent of women were delivered vaginally while primary cesarean section was performed in 36.5%. Thirty-one percent of the neonates were LGA babies. The percentage of macrosomic newborns was 2.9%.

TABLE 1. Baseline demographic and clinical characteristics of study women (N = 345)

Characteristics	n (%)*
Age (years), mean ± SD	34.4 ± 10.7
BMI (kg/m^2), mean ± SD	24.7 ± 5.0
BMI classification	
Normal (18.5-24.9 kg/m^2)	207 (60.0)
Overweight (≥ 25 kg/m^2)	83 (24.1)
Obese (≥ 30 kg/m^2)	55 (15.9)
Nulliparity	141 (40.9)
GA at GDM diagnosis (weeks), mean ± SD	17.9 ± 9.1
Early GDM diagnosis	218 (63.2)
Well-controlled GDM	
Yes	290 (84.1)
No	55 (15.9)
GDM control	
Diet	308 (89.3)
Diet with insulin	37 (10.7)
Risk factors for GDM	
Age ≥ 30 years	286 (82.9)
BMI > 25 kg/m^2	138 (40.0)
Family history of diabetes mellitus	124 (35.9)
History of GDM in previous pregnancy	17 (4.9)
History of DFIU in previous pregnancy	6 (1.7)
History of fetal anomaly in previous pregnancy	9 (2.6)
History of giving birth to macrosomic newborn	7 (2.0)

*unless stated otherwise

Abbreviations: SD = standard deviation; BMI = body mass index; GA = gestational age; GDM = gestational diabetes mellitus; DFIU = dead fetus in utero

TABLE 2. Fetal parameters at 32-36 weeks' gestation (N=345)

Parameters	Mean ± SD	Percentile, n (%)			
		≤ 10th	>10th-50th	51st-< 90th	≥ 90th
BPD (mm)	83.5 ± 4.2	26 (7.5 %)	74 (21.4 %)	119 (34.5 %)	126 (36.5 %)
HC (mm)	303.0 ± 15.1	34 (9.9 %)	74 (21.4 %)	106 (30.7 %)	131 (38.0 %)
AC (mm)	295.8 ± 20.1	23 (6.7 %)	103 (29.9 %)	149 (43.2 %)	70 (20.3 %)
FL (mm)	62.6 ± 3.5	17 (4.9 %)	61 (17.7 %)	143 (41.4 %)	124 (35.9 %)
EFW (g)	2179.6 ± 375.0	56 (16.2 %)	201 (58.3 %)	75 (21.7 %)	13 (3.8 %)

Abbreviations: BPD = biparietal diameter; HC = head circumference; AC = abdominal circumference; FL = femur length; EFW = estimated fetal weight

TABLE 3. Maternal and neonatal outcomes (N = 345)

Outcomes	n (%)*
GA at delivery (weeks), mean ± SD	38.0 ± 1.2
Birth weight (grams), mean ± SD	3,148 ± 466
Delivery route	
Spontaneous vaginal delivery	139 (40.3)
Instrument-assisted delivery	6 (1.7)
Primary cesarean section	126 (36.5)
Repeat cesarean section	74 (21.4)
LGA newborn	107 (31.0)
Macrosomia	10 (2.9)
Birth asphyxia	10 (2.9)
NICU admission	4 (1.2)

*unless stated otherwise
Abbreviations: GA = gestational age; LGA = large-for-gestational age; NICU = neonatal intensive care unit

Univariate analysis for factors associated with LGA newborn in GDM is shown in Table 4. Women with high BMI and women with any fetal parameter of ≥ 90th percentile at 32-36 weeks' gestation were significantly more likely to deliver an LGA baby. All the 13 fetuses with EFW of ≥ 90th percentile at 32-36 weeks' gestation were LGA at birth, resulting in PPV and specificity of 100%. However, the NPV and sensitivity were 71.7% and 12.2% respectively.

TABLE 4. Univariate analysis for factors associated with LGA newborn in GDM

Variables	No LGA newborn (N=238) n (%)	LGA newborn (N=107) n (%)	*p*-value*
BMI			***0.038***
Normal (18.5-24.9 kg/m^2)	150 (72.5)	57 (27.5)	
Overweight (≥ 25 kg/m^2)	58 (69.9)	25 (30.1)	
Obese (≥ 30 kg/m^2)	30 (54.5)	25 (45.5)	
Gestational weight gain			0.345
Below recommended range	99 (69.7)	43 (30.3)	
Within recommended range	78 (72.9)	29 (27.1)	
Above recommended range	61 (63.5)	35 (36.5)	
Nulliparity	98 (69.5)	43 (30.5)	0.863
Multiparity	140 (68.6)	64 (31.4)	
Early GDM	154 (70.6)	64 (29.4)	0.383
Late GDM	84 (66.1)	43 (33.9)	
GDM control			0.116
Well-controlled	33 (60.0)	22 (40.0)	
Poorly-controlled	205 (70.7)	85 (29.3)	
BPD ≥ 90th percentile	66 (52.4)	60 (47.6)	***<0.001***
< 90th percentile	172 (78.5)	47 (21.5)	
HC ≥ 90th percentile	69 (51.9)	64 (48.1)	***<0.001***
< 90th percentile	169 (79.7)	43 (20.3)	
AC ≥ 90th percentile	19 (26.0)	54 (74.0)	***<0.001***
< 90th percentile	219 (80.5)	53 (19.5)	
FL ≥ 90th percentile	72 (55.4)	58 (44.6)	***<0.001***
< 90th percentile	166 (77.2)	49 (22.8)	
EFW ≥ 90th percentile	0 (0.0)	13 (100)	***<0.001***
< 90th percentile	238 (71.7)	94 (28.3)	

*p-value < 0.05 indicates statistical significance

Abbreviations: LGA = large-for-gestational age; GDM = gestational diabetes mellitus; BMI = body mass index; BPD = biparietal diameter; HC = head circumference; AC = abdominal circumference; FL = femur length; EFW = estimated fetal weight

The comparison between groups was performed using Chi-square test.

Multivariate analysis for factors independently associated with LGA newborn in GDM is shown in Table 5. AC and HC of ≥ 90th percentile were independent predictors of LGA newborn with adjusted odds ratio (OR) of 6.5 and 2.0 respecitvely. We determined the adjusted OR of EFW of ≥ 85th percentile because EFW ≥ 90th percentile would produce a "zero" value in calculation formula. EFW of ≥ 85th percentile was the strongest factor of LGA newborn with the adjusted OR of 9.3.

EFW of ≥ 90th percentile resulted in 100% positive predictive value and 100% specificity for identification of fetuses at risk to be born LGA. However, as this cutoff accounted for 3.8% of the fetuses measured at the third trimester, the benefit was limited. In addition, a number of the actual LGA neonates would be missed. Therefore, we tried lower cutoff percentiles in an attempt to increase the sensitivity of third trimester ultrasonography to predict LGA babies. Table 6 shows performance using various cutoffs. Using cutoff levels at 80th and 70th percentile could increase the sensitivity while slightly reducing the PPV and specificity.

Regarding different timing of ultrasonography, no difference of performance in predicting an LGA baby was observed between examination at 32-34 weeks' and 34-36 weeks' gestation.

TABLE 5. Multivariate analysis for factors independently associated with LGA newborn in GDM

Variables	Adjusted OR (95% CI)	*p*-value*
BMI		
Normal (18.5-24.9 kg/m^2)	1	0.253
Underweight (<18.5 kg/m^2)	0.8 (0.4-1.6)	0.53
Overweight and obese (≥25 kg/m^2)	1.6 (0.7-3.5)	0.20
BPD ≥ 90th percentile	1.3 (0.6-2.7)	0.406
HC ≥ 90th percentile	2.0 (1.0-4.0)	***0.048***
AC ≥ 90th percentile	6.5 (3.3-12.8)	***<0.001***
FL ≥ 90th percentile	1.7 (0.9-3.0)	0.059
EFW ≥ 85th percentile	9.3 (1.1-77.9)	***0.038***

*p-value < 0.05 indicates statistical significance

Abbreviations: BMI = body mass index; BPD = biparietal diameter; HC = head circumference; AC = abdominal circumference; FL = femur length; EFW = estimated fetal weight

TABLE 6. Estimated fetal weight (EFW) cutoff percentile for predicting LGA newborn in GDM

Cutoff percentile	PPV (%)	Specificity (%)	Sensitivity (%)	NPV (%)
EFW ≥ 90th percentile	100	100	12.1	71.7
EFW ≥ 80th percentile	90.3	98.7	26.2	74.8
EFW ≥ 70th percentile	88.0	97.5	41.1	78.6

Abbreviations: LGA = large-for-gestational age; GDM = gestational diabetes mellitus; PPV = positive predictive value

DISCUSSION

This prospective cohort study demonstrated that EFW obtained by ultrasound in the third trimester is useful for predicting LGA newborn in women with GDM, especially when all parameters (BPD, HC, AC, and FL) were measured to calculate EFW. Considereing these parameters individually, HC ≥ 90th percentile and AC ≥ 90th percentile were able to predict LGA newborn, with AC being the stronger associating parameter.

The present study found that EFW of ≥ 90th percentile at 32-36 weeks' gestation yielded a PPV of 100%, a specificity of 100%, a NPV of 71.7%, and a sensitivity of 12.2% in prediction of LGA at birth. Previous studies reported lower PPV and specificity with higher NPV and sensitivity,[9,14] whereas the most recent study showed high specificity and low sensitivity, which is similar to our study.[15] The disparity in findings may be due to differences in study population, risk factors, and GDM screening method. Inclusion criteria and the reference growth chart used in other studies were different from ours. Specifically, one study included only women with early GDM and pregestational diabetes,[9] and another used a United States National Reference for Fetal Growth that was published in 1996.[16] The study period during gestation also varied, with one study performing ultrasound during a gestational age range from 28 to 32[6,7] weeks' gestation.[9] In addition, the previously cited studies used EFW percentile cutoffs of 70th, 75th, and 80th percentile, whereas the 90th percentile was used in this study.

The birth weight percentile used in this study was based on 2004-2008 WHO Global Survey on Maternal and Perinatal Health (WHOGS) data,[12] which recruited pregnant women across most countries worldwide, including Thai women. This study, in addition, could be more applicable in clinical practice in comparison to the previous study[14] as the ultrasound was performed during 32-36 weeks' gestation, just after maximal acceleration of fetal growth.

Among various formulas, Hadlock I and III perform best in estimating fetal weight, with Hadlock I having a lower mean absolute percentage error (MAPE).[11,17] Accordingly, Hadlock I formula was used in this study. The present study reveals EFW as the best predictor of LGA newborn in women with GDM. Among all parameters evaluated in this study for estimating fetal weight, AC was found to be the strongest individual predictor of LGA newborn. This finding was similar to that from a previous study which found that AC was the parameter with highest sensitivity. This may be explained by fat accumulation and liver glycogen storage when fetal weight increases in late pregnancy.[18]

This study suggests that the third trimester ultrasound for fetal biometry should be performed in all women with GDM to identify fetus at risk to be LGA at birth. EFW using all parameters (AC, HC, BPD, and FL) provided high PPV and high specificity. However, measuring only AC may be acceptable when measuring all parameters is not feasible due to improper fetal position or difficult maternal habitus.

Despite a high PPV and a high specificity, EFW ≥ 90th percentile had a low sensitivity and low NPV to predict LGA at birth. Lowering to 80th and 70th percentile cutoff values improved the sensitivity and NPV with a slightly reduced PPV and specificity. Concerning gestational age at examination, performance of ultrasonography to predict an LGA neonate was comparable between performing at 32-24 and 34-36 weeks' gestation.

The strengths of the study include its prospective cohort design, and the fact that the reference of EFW was derived from an international standard. A few limitations were also appreciated. Women's glycemic control was only assessed from the values of FBS and 2-h PP blood sugar at antenatal visits, so blood sugar level trends and fluctuations were not examined. Moreover, GDM management during the remaining time before birth could affect the fetal growth.

This study may guide physicians to give special attention for fetuses diagnosed with LGA from ultrasound at a hospital in rural areas for delivery or referral planning in advance.

CONCLUSION

Estimated fetal weight derived from the fetal biometry measured in the third trimester had a high PPV and specificity with a low to moderate sensitivity in predicting LGA at birth.

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Conflict of interest declaration

All authors declare no conflicts of interest.

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