Prediction of fetal macrosomia with ultrasound parameters and maternal glycemic controls in gestational diabetes mellitus

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Summary

Purpose of investigation: Evaluation of ultrasound measurements of fetal adipose subcutaneous tissue (ASCT), abdominal circumference (AC), liver length (LL), and amniotic fluid index (AFI) in prediction of fetal macrosomia (FM) and gestational diabetes mellitus (GDM). *Materials and Methods:* In a prospective clinical trial, 280 pregnant women underwent 100 g oral glucose tolerance test (oGTT) at 28th week of gestation (wg) and measurements of AC, LL, AFI, and ASCT at 32nd, 34th, 36th, and 38th wg. *Results:* For GDM, the best sensitivity was achieved by ACST at 32nd and 34th wg, the best specificity by LL at 32nd wg (90.6%), the best area under the curve (AUC) by LL at 34th wg (0.944). For FM the best sensitivity was achieved by AC at 32th, 34th, 36th, and 38th wg and by ASCT at 34th wg (94.2%), and the best AUC at 38th wg for AC (0.974). *Conclusion:* Ultrasound parameters of glycemic control were good predictors of FM and GDM.

Key words: Gestational diabetes mellitus; Ultrasonography; Fetal adipose subcutaneous tissue; Fetal liver length; Amniotic fluid index; Fetal abdominal circumference.

Introduction

The reported prevalence of gestational diabetes mellitus (GDM) is 30% to 40% in a population of high-risk women for GDM [1]. Fetal macrosomia (FM) is one of the common adverse outcomes associated with GDM. It occurs in a significant proportion of fetuses of women with GDM, despite relatively good glycemic control [2]. A review of articles from different regions of the world with a documented prevalence of FM reveals a wide range (1% - 28%) in different countries. The prevalence was ≤ 3% in Nigeria [3] and Taiwan [4]; whereas Denmark [5] and Croatia [6] had a prevalence of ≥ 20%.

The sonographic diagnosis of FM is imprecise, and false diagnosis is common [7]. The prediction of FM may have considerable effects on obstetric management, even when the estimated fetal weight (EFW) is below the threshold that mandates Cesarean delivery [7]. EFW is based on biometric data (various combinations of femur length, head circumference, abdominal circumference, and other parameters) collected during the ultrasonographic examination and then incorporated into well-established regression formulas. Macrosomia due to GDM is different from FM due to other predisposing factors. Macrosomic infants of GDM 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 healthy mothers [8]. To overcome these drawbacks, alternative ultrasound markers for FM have been proposed which take advantage of the presumed correlation between subcutaneous fat deposition and fetal weight. Some of these markers are also indicators of glycemia control [9] and good predictors of GDM as well [1].

The aim of this study was to evaluate diagnostic performances of ultrasound indicators of glycemia control in prediction of FM and GDM.

Materials and Methods

The study was carried-out in the Institute for Gynecology and Obstetrics, Clinical Center of Serbia, Belgrade. The study population comprised of pregnant women diagnosed with GDM. The exclusion criteria were multiple gestation, confirmed fetal anomaly, pre-pregnancy hypertension, and pathological oral glucose tolerance test (oGTT) values, diabetes mellitus type 1 or 2, age < 18 years, maternal-fetal ABO incompatibility (titer > 1:30), maternal diseases and long-term medical treatments that might have affected glucose metabolism. A total of 280 pregnant women were enrolled in the study. At 28 weeks of gestation (wg), the study participants underwent oGTT and at 32th, 34th, 36th, and 38th wg ultrasound exams, but the sonographers were blinded to the results of the oGTT of study participants. Dating was established by accurate menstrual history confirmed by sonography prior to 20 weeks. The ultrasound exams were performed using a ECO Ceel Toshiba, variable 2-5 MHz transducer (Toshiba Medical Systems, Ltd, Tokyo, Japan) and the Accuvix V100, Medison, variable 2-8 MHz transducer (Medison Co., Ltd, Seoul, Korea). Measurements of fetal adipose subcutaneous tissue (ASCT), fetal liver length (LL), amniotic fluid index (AFI) and abdominal circumference (AC), were measured using standard techniques [10-13].

Table 1. — *Prediction of gestational diabetes mellitus and fetal macrosomia by ultrasound parameters of glycemic control.*

Week		Prediction of GDM					Prediction of FM				
		AUC	p	CO	Sn	Sp	AUC	p	CO	Sn	Sp
32	AC	0.910 (0.88 - 0.94)	< 0.001	300	0.897	0.777	0.953 (0.93 - 0.98)	< 0.001	304.5	0.942	0.882
	ASCT	0.937 (0.90 - 0.97)	< 0.001	7.45	0.936	0.866	0.875 (0.80 - 0.95)	< 0.001	7.45	0.885	0.763
	AFI	0.833 (0.78 - 0.89)	< 0.001	165.5	0.679	0.837	0.857 (0.79 - 0.91)	< 0.001	153.5	0.904	0.654
	LL	0.942 (0.91 - 0.97)	< 0.001	47.5	0.872	0.906	0.882 (0.84 - 0.92)	< 0.001	47.5	0.846	0.811
34	AC	0.903 (0.87 - 0.94)	< 0.001	318	0.923	0.738	0.965 (0.94 - 0.99)	< 0.001	325.5	0.942	0.917
	ASCT	0.931 (0.90 - 0.96)	< 0.001	7.75	0.936	0.797	0.919 (0.88 - 0.96)	< 0.001	7.95	0.942	0.781
	AFI	0.856 (0.80 - 0.91)	< 0.001	156.5	0.872	0.718	0.863 (0.81 - 0.92)	< 0.001	178.5	0.750	0.860
	LL	0.944 (0.91 - 0.97)	< 0.001	49.5	0.885	0.866	0.914 (0.88 - 0.95)	< 0.001	49.5	0.885	0.781
36	AC	0.885 (0.84 - 0.93)	< 0.001	338	0.885	0.757	0.973 (0.96 - 0.99)	< 0.001	344.5	0.942	0.895
	ASCT	0.923 (0.84 - 0.95)	< 0.001	8.25	0.885	0.797	0.952 (0.93 - 0.98)	< 0.001	8.45	0.846	0.904
	AFI	0.856 (0.81 - 0.91)	< 0.001	155	0.846	0.743	0.875 (0.82 - 0.93)	< 0.001	179.5	0.750	0.899
	LL	0.917 (0.88 - 0.95)	< 0.001	51.5	0.936	0.752	0.927 (0.89 - 0.96)	< 0.001	52.5	0.904	0.776
38	AC	0.890 (0.85 - 0.93)	< 0.001	357	0.859	0.782	0.974 (0.96 - 0.99)	< 0.001	364.5	0.942	0.908
	ASCT	0.918 (0.88 - 0.95)	< 0.001	8.55	0.923	0.738	0.953 (0.92 - 0.98)	< 0.001	8.85	0.846	0.947
	AFI	0.834 (0.78 - 0.89)	< 0.001	154.5	0.782	0.767	0.870 (0.81 - 0.93)	< 0.001	168.5	0.750	0.882
	LL	0.914 (0.88 - 0.95)	< 0.001	55	0.879	0.757	0.952 (0.93 - 0.98)	< 0.001	57.5	0.827	0.939

AUC: area under the curve, CO: cut-off, Sn: sensitivity, Sp: specificity.

Statistical analysis

All statistical analyses were performed in SPSS 12.0 (SPSS Inc, Chicago, IL) statistical package. Results are presented as frequency, percent, mean ± SD and median (where appropriate). Cut-off values for AC, ASCT, LL to predict the risk of DM and macrosomia were analyzed by creating ROC (receiver operating characteristic) curves. For every cut-off value, sensitivity and specificity are presented. All p values less than 0.05 were considered significant.

Results

In the population studied, the mean age was 26.6 years (SD was 5.1), primiparity was present in 32.5%, secundiparity in 36.48%, terciparity in 26.07%, multiparity (≥ 4) in 5%, primary school level in 23.93%, high school level in 50.71%, and university level in 25.36%. The prevalence of FM and GDM were 18.57% and 27.86%, respectively.

The diagnostic characteristics of the ultrasound parameters of glycemic control in prediction of GDM were evaluated with ROC analysis (Figure 1). The best sensitivity for the proposed cut-off values were achieved by ACST at 32nd and 34th wg, by LL at 36th wg (93.6%), and ASCT at 38th wg (92.3%). The best specificity was achieved by LL at 32nd wg (90.6%). The best area under the curve (AUC) was achieved by LL at 34th wg (0.94), LL at 32nd wg (0.94), and ASCT at 36th wg (0.92) (Table 1).

The diagnostic performances of the ultrasound parameters of glycemic control in prediction of FM were evaluated with ROC analysis (Figure 2). The best sensitivity for the proposed cut-off values were achieved by AC at 32th, 34th, 36th, and 38th wg (94.2%), and by ASCT at 34th wg (94.2%), best specificity by ASCT at 38th wg (94.7%), while the best AUC were achieved at 38th wg for AC (0.974) (Table 1).

Discussion

The prevalence of FM and GDM in the present study were similar to comparable populations in Europe [5, 6]. The EFW is based on biometric data collected during the ultrasound examination. This exam is often obtained as close to delivery as possible to best estimate the fetal weight at birth. Unfortunately, these late exams have relatively poor positive and negative predictive values for fetal macrosomia, which limits their clinical utility for the individual patient [14-16]. Performing ultrasound exam so close to delivery can also present technical challenges such as decreased amniotic fluid and a fetal vertex well-engaged in the pelvis, which may limit visualization and accuracy. Various investigators have sought to overcome these limitations by performing series of ultrasonographic examinations earlier in the third trimester and predicting EFW on the basis of trends of fetal growth determined from earlier scans [17-19]. These were the reasons for this study design, which included evaluation of ultrasound parameters of glycemic control performed remotely from delivery to predict FM.

Sensitivity of ultrasound parameters of glycemic control in prediction of FM in this study ranged from 75% to 94.2%. Usual cut-off value of AC ultrasound measurement > 35 cm at term as an accurate method in identifying FM with high sensitivity (87.50%) and specificity (84.74%) [20], has lower diagnostic value comparing the proposed cut-off values for AC, ASCT, and LL during 32nd, 34th, 36th, and 38th wg. Also, the utility of the proposed cut-off values were supported by a high AUC on ROC analysis. The best AUC in this study were achieved by LL at 34th wg (0.944), by LL at 32nd wg (0.942), and by ASCT at 36th wg (0.923). ROC curves indicated that measurements of AC, ASCT, and LL are superior to sonographic measurements of other fetal soft tissue (cheek-to-cheek diameter, upper arm subcutaneous tissue, and EFW
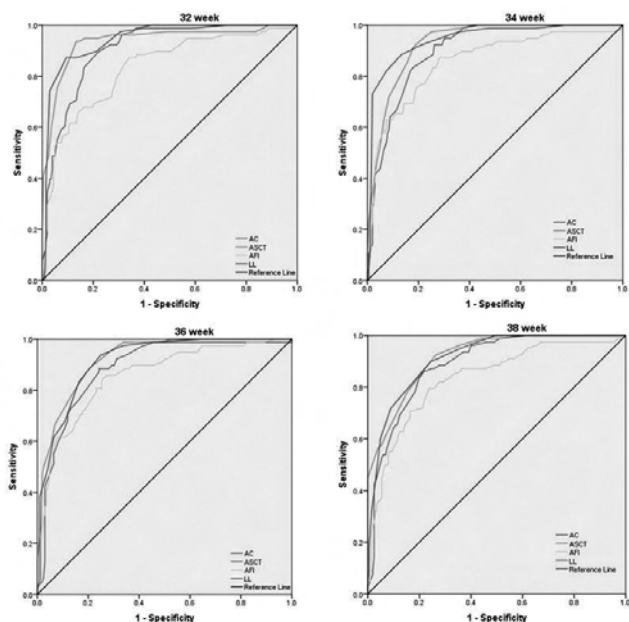
Figure 1. — The diagnostic efficiency of the ultrasound parameters of glycemic control in prediction of FM evaluated by ROC analysis.

Figure 2. — The diagnostic efficiency of the ultrasound parameters of glycemic control in prediction of GDM evaluated by ROC analysis.

derived from it) achieved in the study of Chauhan and colleagues [21], where the AUC was 0.73 and where two methods (upper arm or thigh subcutaneous tissue and ratio of thigh subcutaneous tissue to FL) were poor diagnostic tests (range of AUC 0.52 ± 0.06 to 0.58 ± 0.07). EFW based on upper arm soft tissue thickness and cheek-to-cheek diameter in their study (areas 0.70 and 0.67, respectively) were not better than the present predictions by ASCT, AC, and LL for detecting macrosomic fetuses [21].

Ultrasound screening for fetal biometry and abnormality is widely practiced and has defined sonographic markers of GDM which include those ultrasound parameters of glycemic control evaluated in this study (ACST, AFI, LL and AC). The authors report that their sensitivity ranged from 67.9% to 93.6% and specificity from 71.8% to 86.6%. This is in accordance with their previous study [1], where sensitivity of AC, AFI, and ACST in GDM prediction ranged from 51.5% to 60.6%, whereas specificity ranged from 81.8% to 94.7%. These findings were unexpected, bearing in mind that in previous study the authors had studied a population that had just been diagnosed with GDM, while in the current study, the participants were diagnosed with GDM at 28th wg and treated with dietary regime and moderate physical activity. This confirms that sometimes this regime is insufficient in acquiring good metabolic control, which is in accordance with another previous study [9]. Moreover, Evers concluded that the postprandial glucose excursions are not always reflected in the HbA1c level [22]. Consequently, intermittent hyperglycemia (usually with normal HbA1c) could be more important than chronic hyperglycemia (usually with higher HbA1c) in causing accelerated fetal growth
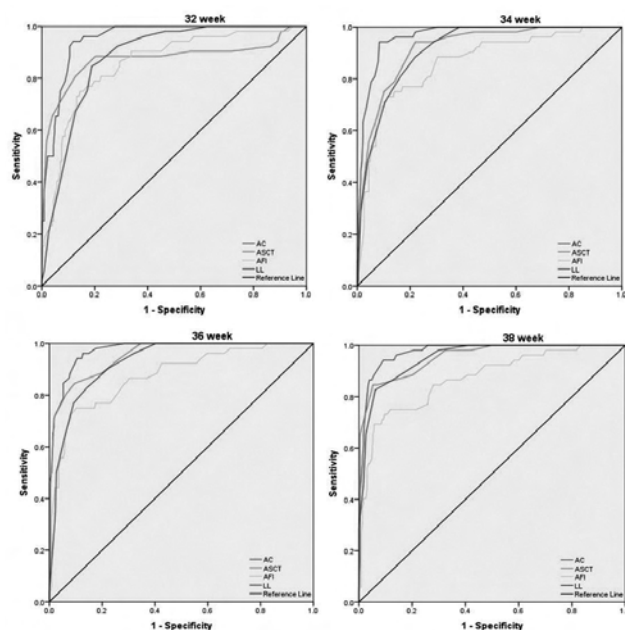
[23]. In addition, Jovanovic stated that "macrosomia despite normoglycemia should rather state macrosomia because of undetected (postprandial) hyperglycemia [24]".

Conclusion

Ultrasound parameters of glycemic control could be an additional tool in predicting FM even more remotely from delivery and term, and also in detection of GDM if this entity is not diagnosed through usual screening periods at 24th to 28th wg because of organizational oversights or other reasons.

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