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Second Trimester Two-Dimensional Sonographic Placental Measurement and Uterine Artery Doppler for Prediction of Adverse Pregnancy Outcome In Low-Risk Pregnancy

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ABSTRACT

Background: Decreased placental volume is associated with higher incidence of small for gestational age (SGA) fetuses and adverse pregnancy outcome (APO). **Objective:** We used two-dimensional sonography to study the association between placental parameters and UAD sonography with APO in a low-risk obstetric population. Singleton pregnant women at 18 to 24 weeks of gestation enrolled the study. Participants underwent 2D sonography. Fetal biometric and placental parameters were measured. Placental volume was calculated using convex-concave shell formula. Mean pulsatility index (PI) ≥ 1.6 or the mean resistance index (RI) ≥ 0.58 or presence of diastolic notch was considered as abnormal UAD. SPSS version 20 was used for data analysis. **Results:** In 508 women with singleton pregnancies, APO was found in 30.4%. Significant correlations of placental height and volume with neonatal weight were found. Mean placental height and volume was lower in SGA than AGA group ($P=0.036$ and 0.034 , respectively). Mean placental thickness and height was lower in APO group than controls ($P=0.030$ and $P<0.001$, respectively). In SGA group, for placental height, the area under the curve (AUC) was 0.678 ($P=0.013$). With cut-off of 3.4 cm, there was 66.7% sensitivity and 62% specificity. In APO group, for placental height, the AUC was 0.714 ($P=0.001$). There were no significant differences in mean PI and mean RI between SGA and AGA groups as well as between APO and normal outcome pregnancies. **Conclusion:** The preferential value of second-trimester placental volume and placental height in predicting SGA compared to Doppler sonography may be concluded.

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INTRODUCTION

Placental insufficiency due to developmental pathologic changes in the placental vasculature results in damaged exchange of gas and nutrients as well as placental size reduction [1]. Investigations have revealed that decreased placental volume is associated with higher incidence of small for gestational age (SGA) fetuses and adverse pregnancy outcome (APO) [2,3]. Nowadays, aptly prediction and recognition of high risk pregnancies in fetomaternal medicine, e.g. SGA and preeclampsia, possess considerable importance. Timely detection of fetal growth restriction (FGR) and fetal surveillance result in better pregnancy outcome and lower morbidity [4]. Respectively, about 4-8% and 6-30% of the newborns in developed and developing countries are growth-restricted.

Appropriate fetal growth depends on supplying of nutrients from mother which need convenient perfusion of uterine artery and exchange of nutrients via placenta and umbilical artery [5,6]. Given to the crucial role of placenta in fetal growth, sonographic evaluation of the placenta would be potentially beneficial in early diagnosis of APO. Some studies have been conducted to develop a screening tool for detection of placental insufficiency to predict SGA including two-(2D) and three-dimensional (3D) sonographic measurements of

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placental volume and uterine artery Doppler (UAD) indices [5]. These studies have mainly done on the high-risk pregnant women. Results show that placental volume and uterine artery pulsatility index (PI) are independent predictors of SGA at mid-pregnancy. Because of the complexity and more expertise needed for placental assessment by 3D sonography, we used 2D sonography to study the association between placental volume, height, width and thickness, maternal and fetal placental surface area as well as UAD sonography with APO in a low-risk obstetric population.

MATERIALS AND METHODS

This prospective study was done from January 2012 to January 2013 in maternal fetal medicine Department of university hospital in Tehran, Iran. Singleton pregnant women at 18 to 24 weeks of gestation referred to our antenatal care unit enrolled the study. Gestational age was calculated from the last menstrual period (LMP) and the first trimester sonography results. Excluded were smokers, those with anemia, fetal anomalies and history of diabetes mellitus or gestational diabetes mellitus, hypertension, placental abruption, intrauterine growth restriction (IUGR), intrauterine fetal demise. Neonates with birth weight less than 10th centile and between the 10th and 90th centile for gestational age compared to normogram were defined as SGA and appropriate-for-gestational age (AGA), respectively. The study protocol was approved by the medical ethics committee of the research deputy of Tehran University of Medical Sciences. Written informed consent was taken from all the participants.

Participants underwent transabdominal 2D sonography with curve-linear transducer by using a 2-5 MHz probe (Acuson Antares, Siemens AG, Germany). Fetal biometry including biparietal diameter (BPD), femoral length (FL), abdominal circumference (AC) and estimated fetal weight (EFW) was done. Placental parameters were measured in a fully seen placental and cord insertion view; placental thickness was measured at the site of cord insertion. Maximal height and width, as well as the maternal and fetal placental surface areas were measured. Placental volume was calculated using convex-concave shell formula: $V = (\pi T/6) * [4H(W-T) + W(W-4T) + 4T^2]$ where V=volume; W=maximal width; H=height at maximal height and T= thickness at maximal height [7].

UAD sonography was also done at both sides at the point of crossover with external iliac arteries. Mean pulsatility index (PI) ≥ 1.6 or the mean resistance index (RI) ≥ 0.58 or presence of diastolic notch was considered as abnormal UAD [8].

For data analysis we used SPSS for Windows, version 20.0 (IBM SPSS Statistics, Chicago, IL, US). Quantitative variables are presented as mean (\pm standard deviation) and 95% confidence interval (CI). Qualitative variables are described as number and percentages. To select cut-point for predicting variables, receiver-operating characteristics (ROC) analysis was performed. Independent samples T-test was used for the comparison of quantitative variables between the groups. Pearson correlation test was used to determine the association between quantitative variables. A P-value < 0.05 was considered significant.

Results:

Totally, 508 women with singleton pregnancies enrolled the study. Table 1 represents the characteristics of the study population. The prevalence of APO was 30.4%; IUGR, pre-eclampsia, preterm labour and stillbirth were found in 20.6%, 2.9%, 17.6% and 2.0% of the pregnancies, respectively. Analyses showed significant correlation of placental height ($r=0.24$, $P=0.016$) and placental volume ($r=0.22$, $P=0.023$) with neonatal weight.

Table 2 shows the comparison of some maternal and fetal variables in the SGA and AGA neonates. According to the Table, SGA and AGA groups were not different in the regard of maternal age and gestational age. The placental thickness, placental width, maternal and fetal surface areas were not different in the groups as well. Mean placental height in the SGA group was lower than AGA group ($P=0.036$). Similarly, mean placental volume was significantly lower in SGA group compared with AGA group ($P=0.034$).

Table 3 provides the comparison of the APO and normal outcome pregnancies. Comparison of groups with APO and normal outcome failed to reveal differences in the regard of maternal age, gestational age, placental width, and maternal and fetal surface areas. But, mean placental thickness in APO group was significantly lower than the normal outcome group ($P=0.030$). Likewise, mean placental height was lower in APO group than the normal outcome group ($P<0.001$).

In SGA group, for placental height, the area under the curve (AUC) was 0.678 (95%CI: 0.558-0.797, $P=0.013$). With cut-off of 3.4 cm, there was 66.7% sensitivity (95%CI: 46.5-56.8%), 62% specificity (95%CI: 51.3-72.7%), 63% accuracy (95%CI: 53.5-72.5%) and relative risk (RR) of 2.55 (95% CI: 1.13-5.75). For the placental volume, the AUC was 0.635 (95%CI: 0.518-0.751, $P=0.059$) (Figure 1).

In APO group, for placental height, the AUC was 0.714 (95%CI: 0.610-0.817, $P=0.001$); the sensitivity was 70% (95%CI: 53.6-86.4%). There were 67.1% specificity (95%CI: 56.1-78.1), 68% accuracy (95%CI: 58.9-77.1%), and a RR of 2.97 (95%CI: 1.51-5.83). For the placental volume, the AUC was 0.624 (95%CI: 0.514-0.734, $P=0.50$).

In the current study, there was significant correlation between the placental height and neonatal weight ($r=0.24$, $P=0.016$) and also between the placental volume and neonatal weight ($r=0.22$, $P=0.023$).

As noted earlier, mean pulsatility index (PI) ≥ 1.6 or the mean resistance index (RI) ≥ 0.58 or presence of diastolic notch was considered as abnormal UAD. Abnormal UAD was reported in 265 out of 508 pregnancies. It was not correlated with neonatal weight, placental height, width and volume. Abnormal UAD was reported in 65 out of 105 pregnancies with SGA; so, the sensitivity, specificity and RR were 61%, 49.4% and 1.5, respectively. In APO group, abnormal UAD was found in 100 pregnancies yielding respectively a sensitivity, specificity and RR of 64%, 52.1% and 1.6. The accuracy of placental height >3.4 cm in SGA and APO groups was 63 and 68 percent, respectively. Accordingly, the accuracy of UAD in SGA and APO groups was 52.9 and 51.9 percent. There were no significant differences in mean PI and mean RI (1.16 vs. 1.07 and 0.59 vs. 0.56, respectively) between SGA and AGA groups. Also, the difference of mean PI and mean RI (1.16 vs. 1.07 and 0.59 vs. 0.55, respectively) between APO and normal outcome pregnancies was not statistically significant.

Table 1: Characteristics of the study population.

	Mean \pm SD	Range
Maternal Age (years)	29.6 \pm 5.7	19-41
Parity (n)	1*	0-4
Gestational age (weeks)	20.0 \pm 2.5	18-24
Maternal weight (Kg)	66.8 \pm 8.1	47-90
Neonatal weight (g)	3045 \pm 720	950-4800

SD=Standard Deviation

* Median

Table 2: Comparison of Maternal and Fetal Variables in the SGA and AGA neonates.

	SGA	AGA	P-value
Maternal age (years)	31.0 \pm 4.2	29.3 \pm 5.8	0.209
Gestational age (weeks)	20.9 \pm 2.5	20.6 \pm 2.0	0.584
Placental thickness (cm)	2.9 \pm 0.7	3.1 \pm 0.9	0.036*
Placental height (cm)	3.3 \pm 1.0	4.0 \pm 1.5	<0.001*
Placental volume (cm ³)	197.7 \pm 74.4	259.1 \pm 124.9	0.034*
Neonatal weight (g)	2276.7 \pm 569.5	3247.8 \pm 592.3	<0.001*

*Significant; SGA=Small for gestational age; AGA= Appropriate for gestational age

Table 3: Comparison of Maternal and Fetal Variables in the APO and Normal Outcome pregnancies.

	APO	Normal Outcome	P-value
Maternal age (years)	31.1 \pm 4.9	29.3 \pm 5.8	0.98
Gestational age (weeks)	20.7 \pm 2.3	20.6 \pm 2.1	0.799
Placental thickness (cm)	2.8 \pm 0.6	3.1 \pm 1.0	0.030*
Placental height (cm)	3.2 \pm 0.9	4.1 \pm 1.5	<0.001*
Placental volume (cm ³)	205.2 \pm 77.3	263.6 \pm 128.8	0.006*
Neonatal weight (g)	2391.6 \pm 663.7	3335.6 \pm 434.9	<0.001*

*Significant; APO=Adverse pregnancy outcome

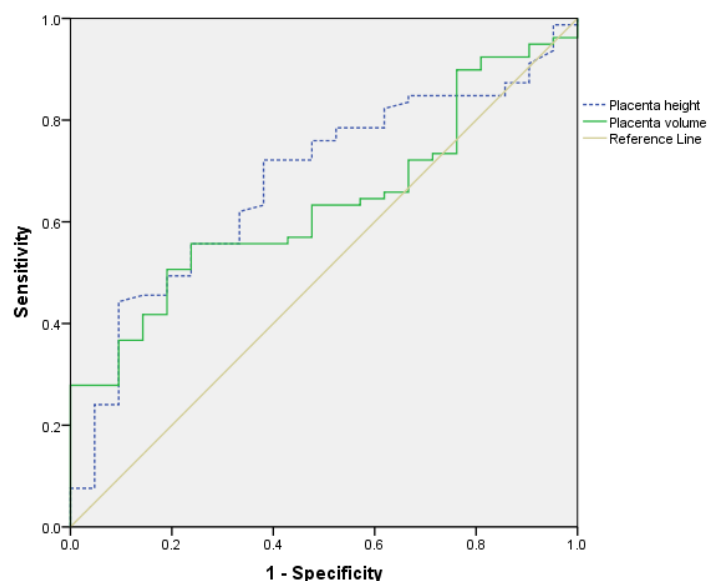


Fig. 1: Receiver-operating characteristics (ROC) curve of placental height and placenta volume in the group of small for gestational age (SGA) neonates.

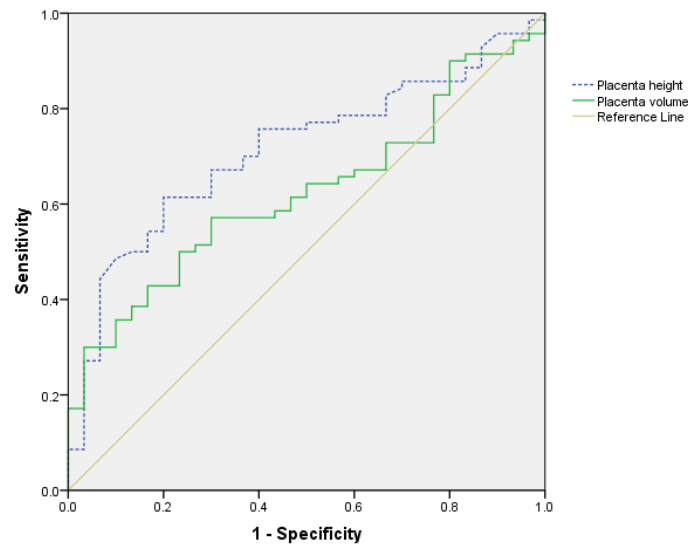


Fig. 2: Receiver-operating characteristics (ROC) curve of placental height and placental volume in the adverse pregnancy outcome (APO) group.

Discussion:

Antenatal detection of pregnancies highly at risk of IUGR, significantly decreases perinatal morbidity and mortality [9]. Some studies have elucidated the relationship between UAD indices and IUGR in the second trimester [10,11]. Predicting the adverse pregnancy outcome (APO), especially SGA, may help reducing mortality and morbidity. Considering the principal role of placenta in the pathophysiology of these outcomes, measurement of the placental parameters may be potentially beneficial in low-risk pregnancies.

There was no significant association between abnormal Doppler sonography findings with neonatal weight in our study. Schuchter *et al.* (2001) studied 380 singleton pregnancies and used Doppler assessment of both uterine arteries as well as 3D ultrasonography to measure placental volume for identifying women at risk of subsequent APO [12]. Schwarze *et al.* (2005) showed limited diagnostic value of UAD for predicting APO; albeit this value increased by performing Doppler studies at 23-26 gestational weeks instead of 19-22 weeks' gestation [13]. A study by Hafner *et al.* (2006) revealed similar sensitivities of calculated placental quotient (placental volume/crown-rump length) at 12 gestational weeks and UAD at 22 weeks for predicting pre-eclampsia and FGR; the authors proposed using this method at the first trimester as well [14].

Our study showed significant relationships between neonatal weight with placental height and placental volume using 2D sonography. Azpurua *et al.* (2010) introduced a simple, practical and accurate method for determination of placental volume using 2D ultrasound [10]. Kinare *et al.* (2000) showed a significant relationship between the birth weight and mid-pregnancy placental volume ($r=0.25$, $P<0.001$). This was independent of maternal weight and was capable to predict the birth weight [15]. In a survey by Adegoke *et al.* (2013) on singleton pregnancies between 36 weeks gestation and delivery, it was shown that 2D sonographic assessment of placental thickness may accurately predict the actual volume and weight of placenta as well as FGR and LBW [16].

In our study, the placental height and volume were significantly different between SGA and AGA groups. Placental volume, placental height and placental thickness were also significantly different between APO and normal outcome groups. Thame *et al.* (2001) demonstrated that fetal size is significantly influenced by both placental volume and the rate of placental growth in the first half pregnancy; and it is probably mediated by maternal height and weight gain. The placental volume was the strongest determinant of birth weight at each age, and improved the prediction based only on fetal measurements. Furthermore, there was an increased odds ratio of LBW by 1.68 (95% CI: 1.05-2.69, $P=0.03$) for every standard deviation decrease in placental volume at 14 weeks' gestation [17]. In a study on 498 singleton pregnancies, placental thickness at the level of cord insertion in the late second and third trimester had positive linear correlations with ultrasonographic gestational age in both groups with outcome fetal weight < 2500 g and ≥ 2500 g. This study suggests that placental thickness at this level may be implemented as a precise indicator of gestational age [18]. Another study done by Afrakhteh *et al.* (2013) on 250 singleton pregnancies also found significant positive correlations between trans-abdominally measured placental thickness and birth weight in the second and third trimesters ($r=0.15$, $r=0.14$, respectively); but its changes could not predict LBW [19]. In a recent retrospective study in Japan, measuring placental thickness by ultrasonography may be a good predictor of APO [20].

Schwartz *et al.* (2012) evaluated 1909 singleton pregnancies. They found that 2D sonographic measurement of placental parameters at 18-24 gestational weeks is significantly associated with the incidence of SGA neonates [5]. McGinty *et al.* (2012) studied 520 singleton low-risk pregnancies at 18-24 gestational weeks and established reference ranges for placental length and thickness. They showed that a placental length <10th centile between the gestational age of 18 and 24 weeks is a significant factor associated with SGA neonate (OR=2.8, 95% CI: 1.1–6.9). An abnormal uterine artery Doppler is a significant factor for SGA neonate (OR=3.4, 95% CI: 1.6–7.4). They proposed that an incorporated single measurement of placental length into the anatomy scan would be helpful in early detection of the pregnancies with a SGA neonate [21].

Conclusion:

The current study emphasizes the role of placental height and volume in predicting the SGA and APO in such pregnancies. Performing sonography for anatomical survey and measuring the placental parameters at 18-22 gestational weeks is an important privilege of this method.

Given to these findings, the preferential value of placental volume and placental height in predicting SGA compared to Doppler sonography may be concluded. With regard to higher sensitivity and accuracy of placental height than Doppler sonography for predicting IUGR, more precise sonographic measurement of placental height at 18-24 gestational weeks is recommended.

In summary, the findings of this study may help more precisely predicting IUGR neonates by measuring placental parameters using 2D-sonography in second trimester of low-risk pregnancies.

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