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Association between first-trimester placental volume and birth weight

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ABSTRACT

Objective: To estimate the correlation between first-trimester placental volume, birth weight, small-for-gestational-age (SGA), and preeclampsia.
Methods: A prospective study of women with singleton pregnancy at 11–13 weeks of gestation was conducted. First-trimester placental volume was measured using three-dimensional ultrasound and reported as multiple of median (MoM) for gestational age. Participants were followed until delivery where birth weight, placental weight, and occurrence of preeclampsia were collected. Non-parametric analyses were performed.
Results: We reached a complete follow-up for 543 eligible women. First-trimester placental volume was significantly correlated with birth weight (correlation coefficient: 0.18; $p < 0.0001$) and placental weight (cc: 0.22; $p < 0.0001$) adjusted for gestational age. First-trimester placental volume was smaller in women who delivered SGA neonates (median MoM: 0.79; interquartile range: 0.62–1.00; $p < 0.001$) and greater in women who delivered large-for-gestational-age neonates (median MoM: 1.13; 0.95–1.49; $p < 0.001$) when compared to women with neonates between the 10th and 90th percentile (median MoM: 1.00; 0.81–1.25). First-trimester placental volume was not associated with the risk of pre-eclampsia (cc: 0.01; $p = 0.87$).
Conclusion: First-trimester placental volume is strongly associated with fetal and placental growth. However, we did not observe a correlation between placental volume and the risk of preeclampsia.

1. Introduction

A newborn small-for-gestational-age (SGA) is a complication of pregnancy commonly related to placental insufficiency [1]. Pre-eclampsia is another complication that is frequently associated with SGA and placental insufficiency, particularly in the early-onset forms of the disease [2]. Over the last decade, there has been a growing interest in the early prediction of SGA and preeclampsia that has been enhanced with the publication of meta-analyses suggesting that most cases could be prevented using low-dose aspirin initiated early in pregnancy [3–5]. While several combinations of biophysical, biochemical, and ultrasonography markers have been proposed, the predictive values remain quite heterogeneous between studies [6–10].

Evaluation of placental size and volume using ultrasound has been proposed to predict the risk of SGA and preeclampsia [11]. At mid-trimester ultrasound, a small placental size or volume has been associated with high risk of SGA [12–16]. Measurement of placental volume as early as the first-trimester has also been related to the development of SGA and preeclampsia, but such associations have been disputed [17–19]. In a large cohort of 3104 singleton pregnancies, Plasencia et al. reported a strong correlation between first-trimester placental volume and birth weight, but they did not report the association with the risk of preeclampsia [18].

In the current study, we aimed to evaluate the value of first-trimester placental volume using 3D Doppler ultrasound for the prediction of SGA and preeclampsia.

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2. Methods

We performed a prospective cohort study of pregnant women from March 2010 to January 2011 after approval from the Ethics Review board of the CHU de Québec. Singleton pregnancies were recruited before 14 weeks of gestation. Multiple pregnancies, fetus with suspected lethal malformation or chromosomal anomalies (posteriori diagnosis) and pregnancies that ended by a spontaneous abortion before 20 weeks, were excluded. After written consent, each woman filled a medical and obstetrical questionnaire. An ultrasound was scheduled and performed between 11weeks + 0 day and 13weeks + 6 days where crown-lump length (CRL) were measured and three-dimensional sweeps of the entire placenta was acquired using Voluson 730 Expert ultrasound machines (GE Medical Systems, Milwaukee, WI, USA) equipped with a 4–8 MHz transducer. Gestational age was determined based on last menstrual period unless the difference with first-trimester ultrasound was greater than 5 days. Participants were followed until delivery and medical records were reviewed for perinatal data including birth weight, placental weight, gestational age, and the presence of preeclampsia. The definition of preeclampsia was that of the International Society for the Study of Hypertension in Pregnancy [20]. Briefly, systolic blood pressure should be 140 mmHg or more and/or diastolic blood pressure should be 90 mmHg or more on at least two occasions 4 h apart after 20 weeks of gestation in previously normotensive women, and there should be proteinuria (300 mg or more in 24 h) or two readings of at least ++ on dipstick analysis of midstream or catheter urine specimens if no 24-h collection was available. Medical record of each case with suspicion of a hypertensive disorder was reviewed and diagnosis validated by a medical doctor (ME). The definition of SGA was birth weight below the 10th percentile according to gestational age and sex of a standard birth weight curve used in our population [21]. The definition of large for gestational age (LGA) was birth weight greater the 90th percentile. Birth weight between the 10th and the 90th percentile was reported as adequate for gestational age (AGA). Placental weight was also reported as MoM for gestational age after calculation of the median for each gestational age subgroup at birth (28–31 weeks; 32–36 weeks; >36 weeks).

First-trimester placental volume was measured for each participant by a single observer who was blinded to all clinical data and using a published technique [17–19]. The VOCAL (Virtual Organ Computer-aided Analysis) was used to obtain a sequence of 6 sections of the placenta, each after a 30° rotation from the previous one. In each of the 6 planes, the contour of the placenta was drawn manually, taking care to exclude the uterine wall. Placental volume was automatically calculated by the built-in scanner software from the areas highlighted in each of the 6 planes. The distribution of placental volume was made Gaussian after logarithmic transformation. The median log10 placental volume was calculated according to CRL categorized into four subgroups: 45–54 mm; 55–64 mm; 65–74 mm; and 75–84 mm. Then, each participant's log10 placental volume was divided by the median log10 placental volume of the corresponding CRL's subgroup; which was reported as the log10 placental volume multiple of median (MoM). Interobserver variability was assessed *a posteriori* on a random sample of 238 cases that were measured by a second observed blinded to the original data.

Spearman correlation test, Mann–Whitney *U* test, and chi-squared test were used to evaluate the correlation between log10 placental volume MoM and each perinatal outcomes: birth weight, birth weight percentile, placental weight, placental MoM for gestational age, and preeclampsia. SPSS 20.0 (SPSS Inc., Chicago, Ill., USA) was used to compute the data. p values below 0.05 were considered significant.

3. Results

A total of 607 women were recruited at a mean gestational age of 12 weeks and 6 days. Of them, 64 women were excluded of the analyses: 47 were not eligible at the time of the 11–13 weeks ultrasound (twins, miscarriage, and wrong gestational age); there were also 5 interruptions of pregnancy for fetal anomalies; 3 cases of fetal miscarriage after recruitment; 7 (1.2%) cases lost to follow-up; and 2 (0.3%) cases that did not have adequate placental tridimensional ultrasound. From the 543 women included in the analyses, 12 (2.2%) developed preeclampsia and 31 (5.7%) delivered an SGA neonate, including 4 women who had combined both preeclampsia and SGA. There was no case of early-onset (<34 weeks) preeclampsia and only two (0.4%) cases of preterm preeclampsia. Table 1 reports the characteristics of each group. We observed that women with SGA neonates without PE were more likely to be smokers, and had a smaller placental weight at birth.

Using Spearman's test, we found that placental volume was significantly associated with CRL ($p < 0.001$), but not with maternal age ($p = 0.22$), maternal BMI ($p = 0.90$) or parity ($p = 0.99$). Fig. 1 shows the distribution of placental volume according to CRL: the median placental volume increases with advancing CRL from 34 ml at CRL of 45–54 mm, to 37 ml at CRL of 55–64 mm, 47 ml at CRL of 65–74 mm and 56 ml at CRL of 75–84 mm. We observed an excellent inter-observer reproducibility for the measurement of placental volume (Pearson coefficient correlation (cc): 0.86; $p < 0.0001$) with a median difference of 4.8 ml (interquartile range: 2.1–9.1 ml) or 9.8% (4.6–17.0%).

First-trimester log transformed placental volume MoM was strongly associated with birth weight (cc: 0.18; $p < 0.001$), birth weight percentile (cc: 0.17; $p < 0.001$); placental weight at birth (cc: 0.21; $p < 0.001$); and placental weight MoM for gestational age (cc: 0.22; $p < 0.001$). SGA neonates were associated with a smaller first-trimester placental volume MoM and LGA neonates were associated with larger placental volume MoM than AGA neonates (Fig. 2). On the other hand, women who developed preeclampsia without SGA had a similar first-trimester placental volume when compared to women without preeclampsia or SGA (Fig. 3).

4. Discussion

We found that first-trimester placental volume as measured by 3D Doppler ultrasound is smaller in women who will deliver an SGA neonate and larger in women who will deliver an LGA neonate. Our data are in agreement with those of Plasencia et al. who previously demonstrated the positive correlation between first-trimester placental volume and birth weight [18]. However, similarly to Odibo et al., we did not confirm the findings of Rizzo et al. who suggest that small first-trimester placental volume was a strong predictor of preeclampsia in the absence of SGA [17,19]. Such differences can potentially be explained by the fact that our study sample had a low risk of preeclampsia (2.1% compared to 4.5% in the Rizzo's study) and much less severe cases (we observed no case of preeclampsia before 32 weeks' compared to 6 (38%) out of 16

Table 1
Characteristics of eligible women.

	No PE – no SGA (reference group)	SGA – no PE	PE – no SGA	SGA & PE
	$N = 504$	$N = 27$	$N = 8$	$N = 4$
Maternal age (years)	30 (27–32)	27 (26–33)	31 (28–35)	29 (27–34)
Body mass index (kg/m^2)	23 (21–26)	23 (20–26)	27 (21–36)	23 (20–26)
Nulliparous (n)	249 (49%)	16 (59%)	6 (75%)	0
Smoker (n)	39 (7.7%)	6 (22%)*	0	0
Crown-rump length (mm)	62 (56–68)	64 (51–69)	60 (58–64)	60 (58–67)
Gestational age at delivery (weeks)	40 (39–40)	39 (39–40)	38 (35–38)*	38 (37–39)
Birth weight (g)	3407 (3120–3730)	2602 (2395–2766)*	2953 (2398–3793)	2398 (1927–2650)*
Placental weight (g)	511 (446–577)	381 (354–453)*	463 (405–619)	426 (290–534)

Continuous variables are reported in median with their interquartile range. *$p < 0.05$.