Low midpregnancy placental volume in rural Indian women: A cause for low birth weight?

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OBJECTIVE: We sought to study midpregnancy placental volume in rural Indian women, its maternal determinants, and its relationship to neonatal size.

STUDY DESIGN: We performed a prospective community-based study of maternal nutrition and fetal growth in 6 villages near the city of Pune. Measurements included midpregnancy placental volume determined by means of ultrasonography at 15 to 18 weeks' gestation, maternal anthropometric measurements before and during pregnancy, and maternal blood pressure and biochemical parameters during pregnancy. Neonatal size and placental weight were measured at birth.

RESULTS: The mothers were short and underweight (mean height, 1.52 m; weight, 42 kg; body mass index, 18 kg/m^2) and produced small babies (mean birth weight, 2648 g). Midpregnancy placental volume (median, 144 mL) was related to the mother's prepregnancy weight ($r = 0.15$; $P < .001$) but not to weight gain during pregnancy, blood pressure, or circulating hemoglobin, ferritin, red blood cell folate, or glucose concentrations. Midpregnancy placental volume was related to placental weight at birth ($r = 0.29$; $P < .001$) and birth weight ($r = 0.25$; $P < .001$) independent of maternal size.

CONCLUSION: In Indian mothers midpregnancy placental volume is significantly associated with prepregnant maternal weight and is an independent predictor of birth weight. Our findings may provide clues to the high prevalence of low-birth-weight infants in India. (Am J Obstet Gynecol 2000;182:443-8.)

Key words: Midpregnancy placental volume, ultrasonography, placental weight, neonatal size, rural India

There is a rising epidemic of diabetes and coronary heart disease in India.[1, 2] The reasons for this are largely unknown, but a recent hypothesis suggests that poor intrauterine growth is an important risk factor.[3, 4] Maternal size and nutrition are important determinants of fetal growth,[5, 6] and in rural India, where the majority (70%) of Indians live, mothers are short and thin because of chronic energy deficiency. Almost one third of the babies born in India are low birth weight (LBW, <2500 g), predominantly because of intrauterine growth restriction.[7] Decreased delivery of nutrients to the fetus by a small placenta is a key factor in the etiology of intrauterine growth restriction.[8] It has been shown that placental growth potential has already been determined by midpregnancy.[9] A study of factors determining placental growth in midpregnancy might help in the understanding of the pathogenesis of intrauterine growth restriction in Indian babies.

In a prospective community-based study of maternal nutrition and fetal growth in 6 Indian villages, we measured midpregnancy placental volume by means of ultrasonography and studied its relationship to maternal characteristics and fetal growth.

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Material and methods

Study area and subjects. The King Edward Memorial Hospital (Pune, Maharashtra, India) has established an outreach program for delivering primary health care to villages near the city of Pune. We studied maternal nutrition and fetal growth in 6 villages approximately 50 km from the city (Dhamari, Karandi, Kendur, Pabal, Pimpale-Jagtap, and Shikrapur; total population, approximately 33,000). Most families in these villages live by farming cash crops. Women work on the farms in addition to doing domestic work and fetching water and firewood. Few are educated beyond the primary school level. A total of 2675 eligible women (married, aged 15-40 years, and unsterilized) were listed by a house-to-house survey.

Prepregnancy measurements. Women were visited every month for the recording of menstrual dates.

A computerized database containing the names, addresses, and menstrual period dates of the women was used to plan each subsequent field visit. Anthropometric measurements (weight, height, head circumference, and skin-fold thickness [triceps, biceps, subscapular, and suprailiac]) was performed every 3 months by standardized techniques. The last set of measurements before pregnancy was used to represent the prepregnant value in the analysis.

Measurements in pregnant women. Women who missed a menstrual period were examined by ultrasonography 18 ± 3 weeks after the last menstrual period. If a singleton pregnancy was confirmed and no fetal anomalies were detected, the mother was enrolled in the study and examined at 18 ± 3 and 28 ± 2 weeks' gestation. Anthropometric measurements were repeated, and blood pressure was measured by a Dinamap (Critikon, Inc) device. Fasting venous blood samples were obtained, and concentrations of the following biochemical parameters were measured: whole-blood hemoglobin measured with a Coulter T540 (Coulter Electronics Limited) analyzer, erythrocyte folate and serum ferritin measured with a radioimmunoassay (Beckton-Dickinson UK, Ltd), serum vitamin C measured with an ascorbate oxidase–orthophenylene diamine assay on a Cobas analyzer,[10] and fasting plasma glucose measured with a glucose oxidase kit on an Abbott Spectrum (Abbott Laboratories) analyzer. At 28 ± 3 weeks' gestation, a 75-g oral glucose tolerance test was carried out, according to the World Health Organization protocol.[11]

Fetal ultrasonographic examination. We visited each village once a week in a van specially designed to carry the ultrasonography machine (Aloka SSD 500, version 8.1) and videotape facility. A curvilinear-array 5-MHz transducer was used for fetal biometric measurements, and a linear-array 3.5-MHz transducer was used for placental volume measurement. The latter was customized to have a foot length of 14 cm, providing a field of vision of 12.5 cm.

Ultrasonographic gestational age was calculated as an average of the predicted age derived from fetal biparietal diameter, head circumference, femur length, and abdominal circumference.[12] Gestational age was derived from the last menstrual period, unless it differed from the ultrasonographic estimate by >2 weeks, in which case the latter was used. Once the gestational age was confirmed to be between 15 and 21 weeks, placental volume was recorded.

Midpregnancy placental volume estimation. We have used the modified parallel planimetric method described and validated by Howe et al.[13] In brief, women were studied in the supine position. With the transducer perpendicular to the couch plane, placental images are videotaped in the following 2 ways: (1) a longitudinal freeze-frame section and (2) a transverse real-time sweep at uniform speed across the woman's abdomen from the pubic symphysis to the uterine fundus. The custom-made software (Digithurst Ltd) digitizes the videotape recording and displays the longitudinal section and 5 equidistant, cross-sectional, transverse sections. The observer marks the placental longitudinal length and traces the margins of cross-sectional images for the transverse area. The software averages the areas of 2 adjacent sections to give the average cross-sectional area of the placental segment bound by these 2 sections. The volume of each placental segment is calculated by multiplying its average cross-sectional area by its longitudinal length. Addition of all the segmental volumes gives the total placental volume.

Each of the placental recordings was analyzed independently by 2 observers (A.S.N. and M.C.C.). While the placental images were traced, care was taken to exclude myometrial contractions, fibroids, and large venous lakes.

Neonatal measurements. Birth weight and placental weight were recorded within 72 hours of delivery. Placental membranes were trimmed, and the umbilical cord was cut flush with the placenta before weighing. Neonatal crown-heel length, occipitofrontal head circumference, abdominal circumference, and thickness of subscapular and triceps skinfolds were measured in a standardized fashion.

Enrollment in the study began in June 1994, and the last baby was delivered in November 1996. The King Edward Memorial Hospital Ethical Committee approved the study protocol, and permission was obtained from local village leaders.

Statistical methods. The mean difference in midpregnancy placental volume measurement by the 2 observers was 1.8 mL (95% confidence interval, 1.0-2.7); a mean of both observers' estimations was used for analysis. Midpregnancy placental volume values were log transformed to satisfy assumptions of normality and adjusted for gestational age at the time of measurement (mean, 16.8 weeks). Neonatal measurements and placental weight at delivery were adjusted for sex and gestational age at delivery (mean, 39.3 weeks). Correlation coefficients were used to study the association between the 2c parameters, and the Student *t* test was used to test differences between groups. Multiple linear regression was used to assess the independent effects of different variables. The data were analyzed by SPSS for Windows 6.1.3 (SPSS, Inc).

Results

Of 2675 women eligible for the study, 2466 (92%) women agreed to take part in the prepregnancy anthropometry rounds; 1102 of the women who participated became pregnant. Of these, 305 women were not enrolled for the following reasons: medical termination of preg-

Table I. Midpregnancy placental volume according to gestational age

		Midpregnancy placental volume (mL)			*Nonfitting placentas**	
Gestation (wk)	*No. examined*	*No.*	*Median*	*10th-90th percentiles*	*No.*	*%*
15-16	22	22	138	85-240	Nil	—
16-17	257	254	141	100-208	3	1.2
17-18	219	211	153	99-206	8	3.6
18-19	113	83	166	112-241	30	26.5
19-20	49	31	204	120-311	18	36.7
20-21	40	16	228	144-338	24	60
TOTAL	700	617			83	11.8

*Nonfitting placentas were those that extended beyond the field of vision of a 12.5-cm probe and could not be measured.

nancy (n = 112), gestation beyond 21 weeks (n = 168), incomplete prepregnancy anthropometric determinations (n = 14), multiple pregnancy (n = 3), and major fetal anomaly on ultrasonographic examination (n = 8). Of the 797 women enrolled, 12 aborted, 14 had a late medical termination of pregnancy, 1 died of pregnancy-induced hypertension, and 770 were delivered of their infants.

Only 700 of these mothers had midpregnancy placental volumes measured because the special 3.5-MHz linear transducer became available 2 months after the main study had started and 17 midpregnancy placental volume recordings were excluded for technical reasons.

Table I shows that midpregnancy placental volumes increased with gestational age and that there was considerable variation at each gestation. Eighty-three placentas spread beyond the field of view of the linear transducer, and midpregnancy placental volume could not be measured. The proportion of such placentas increased progressively with increasing gestation (2.2% between 15 and 18 weeks and 35.6% between 18 and 21 weeks). The distribution of midpregnancy placental volume and its relationship with maternal parameters is therefore analyzed only for those placentas measured between 15 and 18 weeks of gestation (n = 487). Possible implications of the nonfitting placentas are discussed in a subsequent article.

Between 15 and 18 weeks' gestation, the median midpregnancy placental volume was 144 mL (10th and 90th percentiles, 99 and 207). Placentas positioned on the posterior wall (n = 197) were larger than those on the anterior wall (n = 244; mean, 154 vs 137 mL; $P < .001$).

Relations of midpregnancy placental volume to maternal measurements. Table II shows the characteristics of the mothers. There were no significant differences in measurements of mothers who were excluded and those studied. Midpregnancy placental volume was not related to maternal age (mean, 21 years [SD, 3.5]). It was significantly larger in women with >3 previous pregnancies (n = 14) compared with the remainder of the subjects (mean, 184 vs 143 mL; $P < .001$). Midpregnancy placental volume was positively related to maternal prepregnant weight ($r = 0.15$; $P < .001$) and to maternal weight at the time of the study ($r = 0.12$; $P < .001$) but not to weight gain at any time during pregnancy or to maternal height, head circumference, and skinfold thickness measurements. Midpregnancy placental volume did not correlate with maternal blood pressure or with concentrations of any of the biochemical parameters measured—hemoglobin, ferritin, erythrocyte folate, glucose, and vitamin C. Two mothers had gestation-related impaired glucose tolerance, and one had pregnancy-induced hypertension. The midpregnancy placental volumes in these women did not differ significantly from those of the remainder of the women (139, 168, and 169 mL, respectively).

Table II. Characteristics of mothers

	No.	*Mean ± SD*
Prepregnant		
Weight (kg)	487	42 ± 5
Height (cm)	487	152 ± 5
Head circumference (cm)	475	52.2 ± 1.5
Body mass index (kg/m^2)	475	18 ± 1.9
15-18 wk gestation		
Weight gain (kg)	487	1.6 ± 2.7
Blood pressure		
Systolic (mm Hg)	487	115 ± 9
Diastolic (mm Hg)	487	62 ± 8
Hemoglobin concentration (g/dL)	466	11.5 ± 1.5
Serum ferritin (μg/L)	462	13 (8-23)*
Erythrocyte folate (μg/L)	449	400 ± 170
Fasting plasma glucose (mg/dL)	423	71 ± 12
Serum vitamin C (mmol/L)	422	15 (4.7-35.2)*

*Median and interquartile range.

Midpregnancy placental volume and birth outcome. Among the 487 deliveries, 5 were stillbirths and 5 babies had major congenital anomalies. Midpregnancy placental volumes in the mothers of stillborn babies were smaller than those in women who were delivered of live babies (mean, 110 vs 145 mL; $P = .03$). Midpregnancy placental volume was not related to the sex of the baby or to gestation at delivery. Of the 477 normal live births, birth measurements were available in 443. Forty-seven babies born prematurely (<37 weeks) and 5 born post-

Table III. Correlations between midpregnancy placental volume and neonatal size (term babies)

Birth parameter	*No.*	*Mean ± SD*	*r*	*Statistical significance*
Birth weight (g)	391	2648 ± 314	0.25	*P* < .001
Crown-heel length (cm)	389	47.6 ± 1.8	0.16	*P* = .001
Head circumference (cm)	389	33 ± 1.1	0.18	*P* < .001
Abdominal circumference (cm)	389	28.6 ± 1.8	0.18	*P* < .001
Subscapular skinfold thickness (mm)	389	4.2 ± 0.8	0.12	*P* = .02
Triceps skinfold thickness (mm)	389	4.2 ± 0.8	0.21	*P* < .001
Placental weight (g)	367	357 ± 71	0.29	*P* < .001

All birth parameters were adjusted for gestational age (39.3 weeks) and sex of the baby.

maturely (>42 weeks) were excluded from the analysis of the relationship between midpregnancy placental volume and neonatal parameters, which is restricted to 391 term babies.

Midpregnancy placental volume was significantly related to placental weight at delivery. Birth weight and other neonatal measurements (crown heel length, head and abdominal circumferences, and subscapular and triceps skinfold thickness) were positively related to midpregnancy placental volume (Table III). Midpregnancy placental volume was smaller in LBW babies (<2500 g, n = 127) compared with the remainder (mean, 131 vs 149 mL; *P* < .001). The relationship between midpregnancy placental volume and birth weight remained significant after allowance for placental weight at delivery (*P* < .01).

Similarly, the relationship between midpregnancy placental volume and birth weight remained significant after allowance for fetal measurements made at the same time. Between 15 and 18 weeks' gestation, the mean head circumference, abdominal circumference, and femur length were 13.6, 10.7, and 2.2 cm, respectively. Table IVA shows that midpregnancy placental volume predicted birth weight more strongly than did fetal head circumference and femur length measured at the same time. Even though the abdominal circumference showed a similar degree of correlation with birth weight, the relation between midpregnancy placental volume and birth weight remained highly significant independent of this relationship.

Midpregnancy placental volume and maternal-fetal size relationships. Maternal prepregnant weight, height, and head circumference, all predicted birth weight. Table IVB shows that the relationship between midpregnancy placental volume and birth weight remained significant after allowance for all maternal measurements in the multiple regression analysis. Similarly, the relationship of midpregnancy placental volume with neonatal length and head circumference was independent of maternal height and maternal head circumference, respectively (*P* < .01 for both).

Comment

To our knowledge, this is the first description of placental size measurements in midpregnancy from India. We confirm the relationship between placental size in midpregnancy and the baby's weight and placental weight at term in these undernourished mothers, which has been previously described in mothers from developed countries.[14] The relationship between placental size in midpregnancy and birth parameters was independent of maternal size before pregnancy or weight gain during pregnancy. Midpregnancy placental volume was a significant predictor of LBW and stillbirth. Midpregnancy placental volume was related not only to birth weight but also to other measures of fetal growth. At a given maternal weight, height, or head circumference, a smaller midpregnancy placental volume was associated with smaller birth weight, neonatal length, and head circumference. Similarly, the relationship between midpregnancy placental volume and birth weight remained significant after allowance for placental weight at birth. This suggests that placental growth in early pregnancy is an important and independent predictor of fetal growth.

Ours is an observational study, and it is not possible to say whether small midpregnancy placental volume is the cause of LBW in Indian babies. However, animal experiments have demonstrated that a reduction in placental size in early pregnancy causes a reduction in birth weight.[15] Thus it would not be unreasonable to speculate that small midpregnancy placental volume in Indian mothers could be responsible for the LBW of their babies.

There are not many studies of measurement of placental volume in midpregnancy. We compared our results with those from Southampton, where midpregnancy placental volume was measured by the same technique.[13] At 17 weeks' gestation Indian fetal size was not very different than that of the Western babies[12]; head circumference was >95% and abdominal circumference and femur length were 91% of the Western standards. Placental size, however, was considerably smaller at this stage (71% of midpregnancy placental volume in Southampton [median, 214 mL at 17 weeks' gestation]).[13] At birth, the Indian fetuses grew to be smaller babies compared with babies in Southampton (birth weights of 2653 vs 3440 g, 77% of Southampton),[16] and placental weight was lower (367 vs 533 g, 69% of Southampton).[16]

In our study prepregnant weight was the only maternal characteristic associated with midpregnancy placental

Table IVA. Multiple regression analysis of birth weight (dependent variable) with measurements of midpregnancy placental volumes and fetus at same time

*Parameter**	*r*	*Birth weight†*	*95% Confidence interval*	*Statistical significance*
Midpregnancy placental volume (10 mL)	0.2	14.8	7.82 to 21.82	$P < .001$
Head circumference (cm)	0.04	28.84	–37.89 to 35.58	$P = .39$
Abdominal circumference (cm)	0.16	113.96	47.84 to 180.09	$P < .001$
Femur length (cm)	–0.07	–211.23	–460.5 to 38.06	$P = .09$
Constant		1284.09	759.29 to 1809	$P < .001$

Birth weight was adjusted for gestation at delivery and sex of the baby.
*Parameters adjusted for gestational age (16.8 weeks).
†Change in birth weight (in grams) per unit change in predictor variables.

Table IVB. Multiple regression analysis of birth weight (dependent variable) with midpregnancy placental volume and prepregnancy maternal parameters

Parameter	*r*	*Birth weight**	*95% Confidence interval*	*Statistical significance*
Midpregnancy placental volume (10 mL)†	0.2	13.19	6.64 to 19.73	$P < .001$
Weight (kg)	0.06	4.41	–2.6 to 11.43	$P = .22$
Height (cm)	0.11	7.17	0.58 to 13.75	$P = .03$
Head circumference (cm)	0.11	23.27	2.72 to 43.83	$P = .03$
Constant		–28.09	–1333 to 1277	$P = .96$

Birth weight was adjusted for gestation at delivery, sex of the baby, and maternal parity.
*Change in birth weight (in grams) per unit change in predictor variables.
†Midpregnancy placental volume adjusted for gestational age (16.8 weeks).

volume. Maternal weight gain during pregnancy was not related. Despite gross differences in neonatal and placental size, the relationship between midpregnancy placental volume and maternal weight was similar in our study and the Southampton study (midpregnancy placental volume, 3.64 mL/kg maternal weight in rural Indian babies vs 3.31 mL/kg maternal weight in Southampton). This suggests that the mother's nutrition before pregnancy is an important determinant of early placental growth, and her nutrition in pregnancy may not be a factor. This could have important implications in planning interventions for improving fetal growth.

Previously described inverse relationships between maternal circulating hemoglobin and ferritin concentrations with midpregnancy placental volume[17] were not found in our study. In fact, we did not find significant relationships between any biochemical parameter and midpregnancy placental volume. The reasons for this are not clear. The only other maternal characteristic associated with midpregnancy placental volume was increasing parity of the mother, possibly reflecting changes in uterine size and circulation related to previous pregnancies.

In American women Clapp et al[14] have reported placental volumes similar to those in our study (mean, 130 mL at 16 weeks) in mothers who weighed 59.7 kg and were accustomed to a heavy exercise program. Apart from the measurement technique (static B scanner in American study), the main difference from Southampton women was the high level of physical exercise in the American women. In this respect rural Indian women in our study were also involved in heavy physical activity during their daily life. An average woman in our study cooked for the family, fetched water and firewood from distant sources, looked after the domestic animals, and helped in farm work. This heavy physical activity continued almost up to term.

The midpregnancy placental volume in rural Indian women and American women performing heavy exercise is strikingly similar. However, the American women have considerably smaller placental volume in relation to maternal weight (2.17 mL/kg maternal weight) than both the Indian and the British women. The placentas remained small in Indian women, whereas they caught up in the American women (456 g), although remaining lower than those in the British population. Despite differences in midpregnancy placental volumes, birth weights in the American and the British babies were similar and distinctly higher than those found in the Indian babies.

At present, it is difficult to advocate use of midpregnancy placental volume estimation as a routine clinical tool. The measurement requires a special transducer and takes about 15 minutes to perform. Abdominal circumference, a routine measurement, predicts birth weight equally well. A combined measurement of placental size and abdominal circumference will identify a larger number of fetuses at risk of LBW. We will need to investigate whether a simpler measure of placental size in early pregnancy will be as useful as midpregnancy placental volume in predicting LBW.

In conclusion, we have measured midpregnancy placental volume in a community-based study of rural pregnant Indian women. Midpregnancy placental volume was considerably smaller in Indian women than in women from Southampton but was similar to that found in American women accustomed to heavy exercise. Midpregnancy placental volume in Indian women was related to maternal prepregnant weight and independently predicted LBW. Thus poor placental growth in early pregnancy could at least partly explain the LBW in Indian babies.

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