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Article

Ultrasound measurement of fetal size in rural Guatemala

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Abstract

Objectives: To describe the fetal growth pattern of a population from rural Guatemala and determine when during gestation growth faltering becomes evident. *Methods:* Ultrasound examinations were conducted for 319 women. Femur length (FL), biparietal diameter (BPD), abdominal (AC) and head circumference (HC) were compared with reference values. *Results:* FL and AC were similar to reference values throughout gestation. BPD and HC were below the 50th percentile by 30 weeks' gestation and below the 10th percentile later in gestation. We expected all four dimensions to show marked growth restriction during gestation. Measurement differences may explain the results but would call into question the value of cross-study comparisons. Infants born small for gestational age were small in all measures as early as 15 weeks. *Conclusions:* Fetal growth faltering begins in early gestation among infants who were born small. The lack of deviation from reference data for FL and AC requires further clarification.

Keywords: Ultrasound; Fetal size; Birth size; Guatemala; Rural; Developing country

1. Introduction

Ultrasound measurement for the purpose of gestation dating and the detection of fetal abnormalities is now a routine part of obstetric care in most developed countries. In rural areas of developing countries, where a large percentage of infants are born small, fetal growth failure often remains undetected until birth. Recent studies report data from diverse populations [1–4] but are typically urban and hospital-based, thus capturing mainly middle or higher socioeconomic status groups. Ultrasound is still relatively uncommon in rural areas of developing countries, and, to our knowledge, no systematic assessment of fetal growth using ultrasound has been conducted in a marginally malnourished, rural population.

The etiology of fetal growth failure in poor societies, and its consequences in the short and long term has been reported extensively in the literature. We know that, on average, birth weight, length and head circumference are smaller in infants delivered to poor, rural women when compared to infants of women from urban, higher

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socioeconomic groups of the same ethic origin living in the same country [5,6] or to international reference data [7,8]. A higher prevalence of intrauterine growth restriction (IUGR) has been reported in most rural areas of developing countries than in industrialized countries [9,10] and the relationship between poor maternal nutritional status and restricted fetal growth is well documented [10].

In Guatemala, up to 50% of infants are born with small crown–heel length for gestational age and approximately 20% are born with low weight for gestational age. We do not know when during gestation differences in fetal size between infants born small and adequate for gestational age become manifest. Knowing when growth failure becomes detectable could have important implications for the timing of interventions during pregnancy to prevent fetal growth failure and for the use of ultrasound for pregnancy dating. For example, if the fetuses of marginally malnourished women have notably smaller head size in early gestation, the comparison of biparietal diameter to standard reference tables to estimate gestational age may result in an under-estimate of age due to small fetal size.

This analysis uses cross-sectional and longitudinal data of fetal growth measured by ultrasound in rural Guatemala. Our purpose is to describe patterns of growth as well as to determine when during gestation growth faltering can be detected.

2. Subjects and methods

2.1. Recruitment and birth measures

All women between 19 and 34 years of age from four rural villages in eastern Guatemala were visited in their homes every three months from August 1996 until June 1999 and asked to recall the date of their last menstrual period (LMP). Pregnancy was identified as a missed menstruation and confirmed by clinical assessment conducted by a physician. All pregnant women were invited to participate in a longitudinal study and those interested signed an informed consent declaration. They received free prenatal care (at a mean of 11, 20, 30 and 37 weeks) from field staff nurses of the Institute of Nutrition of Central America and Panama. Two ultrasound exams were programmed for each woman, with additional ultrasound measurements taken during exams that were scheduled for obstetric follow-up reasons.

Women and infants were weighed on an electronic scale (Model 1582, Tanita Corp., Arlington Heights, IL), and height and crown–heel length measured using a portable stadiometer/infantometer (Schorr Productions, Glen Burney, MD). Newborns were measured within 48 h of birth. The current analysis includes the sub-set of women who had at least one ultrasound exam conducted any time during pregnancy, singleton pregnancy and infant born without congenital anomalies.

2.2. Gestational age estimation and ultrasound measurements

An accurate estimate of gestational age, independent of ultrasound measurements to avoid errors in age related to fetal size is essential for meeting the study objectives. Therefore, for this analysis we estimated gestational age based on recalled date of LMP and included only those that resulting in a gestational age at birth within acceptable limits (≤43 weeks).

Fetal measurements were made using real-time ultrasound on a portable machine (Medison Eureka 600, Medison Inc., Seoul, South Korea) equipped with a 3.5 MHz transducer at a velocity of 1540 m/s. Scanning continued until an adequate image was encountered, that image was frozen and measures made using the machines' electronic caliper. Repeat measures were taken from separate scans; three measures within 2 mm for BPD and femur length, two measures within 2 mm for tibia and humerus length and, two measures within 8 mm for head and abdominal circumference. One of two trained obstetricians made all the ultrasound measurements. Ultrasound results were also recorded on a report form, which was given to the participant for her information and medical follow-up.

Biparietal diameter was measured from the outer edge of the proximal parietal bone to the inner edge of the distal parietal bone [11]. Femur length

Table 1
Maternal anthropometric measures before pregnancy and infant anthropometry and gestational age at birth[a]

	N	Mean ± S.D.
Gestational age, weeks	319	39.5 ± 1.8
Birth weight, kg	284	3.06 ± 0.46
Birth weight Z score[b]	283	−0.47 ± 1.02
Birth length, cm	267	48.3 ± 2.0
Birth length Z score[b]	265	−1.01 ± 0.98
Maternal age, years	319	25.9 ± 4.5
Maternal height, cm	313	149.6 ± 5.5
Maternal pre-pregnant weight, kg	262	52.9 ± 10.0

[a] Includes all mother–infant pairs ($n=319$) who met the inclusion criteria, regardless of whether pregnancy and birth information was complete. Therefore, n for measures will differ.

[b] Based on sex- and gestational-age specific reference of Miller and Hassanein [14].

was measured according to the method of O'Brien and Queenan [12] and tibia and humerus length according to the method described by Hansmann and co-workers [13]. Head and abdominal circumferences were measured based on ellipse fitting using standard techniques [11].

2.3. Statistical analysis

Ultrasound measures of fetal size are presented as tables of means and standard deviations for week of gestation with sexes combined to facilitate comparisons with published references. The comparisons between the current data and the reference values are presented graphically for the entire sample. We also related fetal size to newborn size. Z scores (actual measure–reference mean/refer-

Table 2
Head and abdominal measurements by week of gestation

Weeks of gestation	Biparietal diameter[a] (mm)			Head circumference (mm)			Abdominal circumference (mm)		
	N	Mean	S.D.	N	Mean	S.D.	N	Mean	S.D.
14	8	29.1	3.4	5	113.2	8.6	5	98.4	10.4
15	43	30.9	2.7	39	115.4	9.3	39	99.2	9.2
16	73	34.1	3.1	69	124.9	10.5	67	108.8	10.1
17	47	38.5	5.4	44	137.8	10.9	45	121.3	10.7
18	23	39.8	3.2	23	145.3	12.1	23	127.0	14.4
19	13	42.9	3.0	13	158.2	11.7	13	141.9	16.9
20	14	48.6	2.8	14	176.2	6.7	14	158.4	8.6
21	22	49.8	3.3	22	181.3	16.3	22	161.0	12.9
22	8	55.0	7.4	8	200.5	28.7	8	172.9	14.8
23	NR			NR			NR		
24	11	57.7	11.1	11	212.4	39.1	11	195.2	41.2
25	5	64.0	4.3	5	236.2	21.5	5	213.4	24.7
26	NR			NR			NR		
27	NR			NR			NR		
28	20	71.4	3.8	19	260.1	11.3	19	242.4	11.8
29	69	74.7	3.7	68	272.2	11.6	68	256.4	17.7
30	149	76.9	3.8	148	280.0	12.0	148	259.5	20.6
31	39	77.4	3.8	38	281.1	13.3	39	263.8	17.3
32	15	80.7	3.2	15	290.6	12.0	15	279.5	21.9
33	9	80.7	6.1	8	295.0	18.7	9	280.8	20.4
34	13	83.5	5.8	12	304.8	16.6	12	305.3	34.4
35	12	87.9	4.0	11	312.8	14.2	11	313.3	23.7
36	23	85.8	4.1	23	316.0	14.2	22	310.4	28.3
37	17	86.4	5.3	15	317.6	22.7	16	322.6	30.0
38	6	87.5	2.1	6	314.3	9.9	5	326.6	13.5

NR, data not reported for gestational ages with $n<5$.

[a] Measured from the outer edge of the distal parietal bone to the inner edge of the proximal parietal bone.

Table 3
Long bone measurements of the leg and arm by week of gestation

Weeks of gestation	Femur length (mm)			Tibia length (mm)			Humerus length (mm)		
	N	Mean	S.D.	*N*	Mean	S.D.	*N*	Mean	S.D.
14	6	17.3	2.7	4	13.5	1.9	–		
15	39	18.8	2.9	37	15.0	2.9	35	18.7	3.1
16	71	20.8	2.8	60	17.8	2.7	63	21.0	3.0
17	46	24.7	4.9	41	20.0	3.0	42	24.6	3.2
18	23	26.2	3.8	21	21.6	3.7	21	25.9	3.7
19	13	29.1	2.5	13	25.8	3.2	13	28.8	2.8
20	14	33.6	3.0	14	29.3	2.2	14	32.9	3.1
21	22	34.6	1.9	20	30.8	2.6	19	34.2	2.9
22	8	38.9	5.9	8	35.1	5.7	8	36.5	5.4
23	NR			NR			NR		
24	11	43.3	9.6	10	38.5	9.0	10	40.1	7.7
25	6	47.4	4.8	5	42.4	5.0	5	43.8	3.3
26	NR			NR			NR		
27	NR			NR			NR		
28	19	55.1	2.0	17	47.6	3.0	18	49.3	1.8
29	69	57.0	2.9	64	49.8	3.5	66	50.7	23.0
30	149	58.5	2.8	144	51.1	2.9	144	51.9	3.1
31	39	58.8	3.4	38	51.6	3.4	37	52.0	3.5
32	15	62.0	3.9	15	54.4	3.6	15	55.1	3.8
33	9	62.4	3.7	7	54.1	2.9	8	54.3	3.2
34	13	66.1	4.9	12	54.7	5.9	12	59.2	4.0
35	11	68.6	3.3	9	60.1	3.9	11	60.4	2.3
36	23	70.5	4.0	21	60.9	4.0	22	62.0	3.1
37	17	70.9	4.9	14	60.5	4.3	14	61.9	6.3
38	6	72.7	3.7	NR			NR		

NR, data not reported for gestational ages with $n<5$.

ence standard deviation) for birth weight and birth length were calculated based on the reference of Miller and Hassanein [14]. Infants whose length for gestational age at birth fell below the tenth percentile were considered short for gestational age and weight for gestational age less than the reference tenth percentile were classified as small for gestational age (SGA).

Ultrasound measures of biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), and femur length (FL) were converted to *Z* scores using the gestational age specific mean and standard deviation from a population from London, England [15–17] and were compared between SGA and non-SGA infants. This reference was chosen because it provides information on most of the measures presented in this study and ultrasound measurement techniques were similar to ours. Mean *Z* scores for BPD, HC, AC, and FL are presented for the second (15–22 weeks' gestation), early third (29–32 weeks), and late third (35–38 weeks) trimesters. The measurements were grouped in this fashion to increase sample size at each period and are compared by *t*-tests for SGA and non-SGA infants. *P*-values <0.05 were considered statistically significant.

This study received clearance from the Cornell University Committee for Research on Human Subjects, and the Research Subjects Committee at INCAP. Statistical analyses were conducted on a personal computer using SAS for Windows Version 6.12 (SAS Institute Inc., Cary, NC).

3. Results

Ultrasound exams were conducted for 319 women. Data are available for two repeat exams for 158 (49.5%), three exams for 77 (24.1%), four

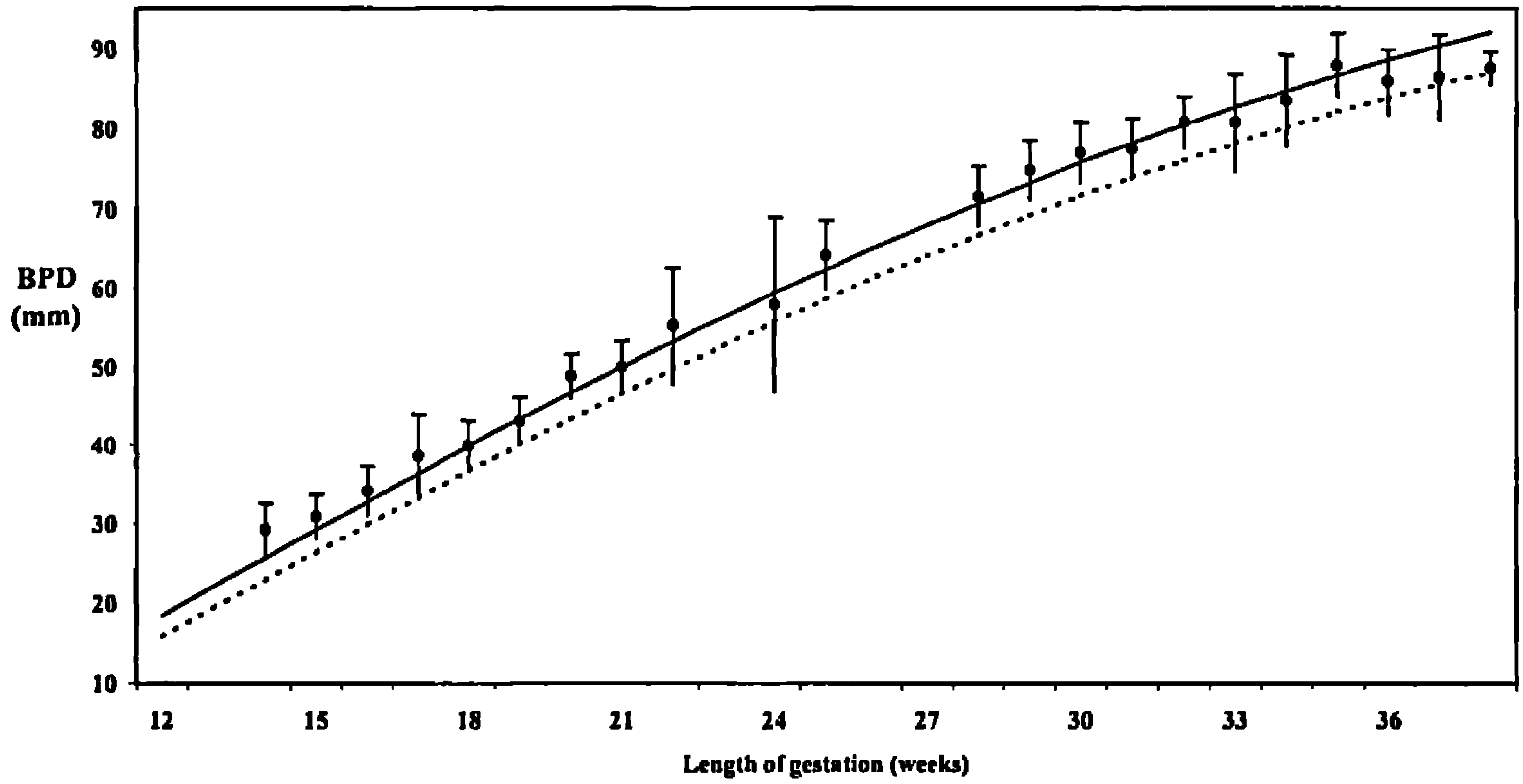

Fig. 1. Biparietal diameter (BPD; mm) for week of gestation compared with reference 10th (dashed line) and 50th (solid line) percentile [15]. Data for Guatemalan sample (mean ± S.D.) are shown when $n > 5$.

exams for 15 (4.7%), and five exams for two (0.6%) women. The remaining 67 (21.0%) women had one ultrasound exam during the pregnancy. Maternal and newborn anthropometry is shown in Table 1.

No differences between the sexes were found before 30 weeks gestation but by 30–31 weeks, male fetuses had larger BPD, HC, and longer humerus ($P < 0.05$) (data not shown). Means and standard deviations by week of gestation for the sexes combined are presented in Table 2 for BPD, HC, and AC and in Table 3 for femur, tibia, and humerus length.

BPD (Fig. 1) and HC (not presented) show a growth pattern very similar to the reference median up to approximately 30 weeks after which both measures are smaller compared with the reference. Mean values for AC (not presented) and FL (Fig. 2) in this population are at or above the reference 50th percentile throughout gestation. Published values for FL in populations from Papua New Guinea [2], Australia [18], and India [4] are compared with the Guatemalan sample and the London reference data [16] in Fig. 2.

Seventy-five infants (22.7%) were classified as SGA and 127 (38.4%) were born with short length for gestational age. The prevalence of preterm birth (<37 weeks) was 5.7% ($n = 19$). SGA infants were shorter in length ($P < 0.01$) but had similar mean gestational age compared with non-SGA infants. Infants were born SGA had significantly ($P < 0.05$) smaller BPD and HC by 30 weeks gestation and significantly ($P < 0.05$) smaller FL and AC throughout gestation compared to their non-SGA counterparts (Fig. 3).

4. Discussion

In rural areas of developing countries, the causes of faltering growth in utero differ from those in developed countries and the prevalence of IUGR and short length for gestational age at birth are considerably higher. Ultrasound measures in such populations should, therefore, be smaller than reference values from healthy, developed country populations at some point during gestation. Information on fetal growth patterns in such populations is useful to understand the timing of intrauterine growth faltering and may assist in the design of effective, timely interventions to reduce the prevalence of IUGR. Finally, as ultrasound becomes more economical and accessible, it is essential to

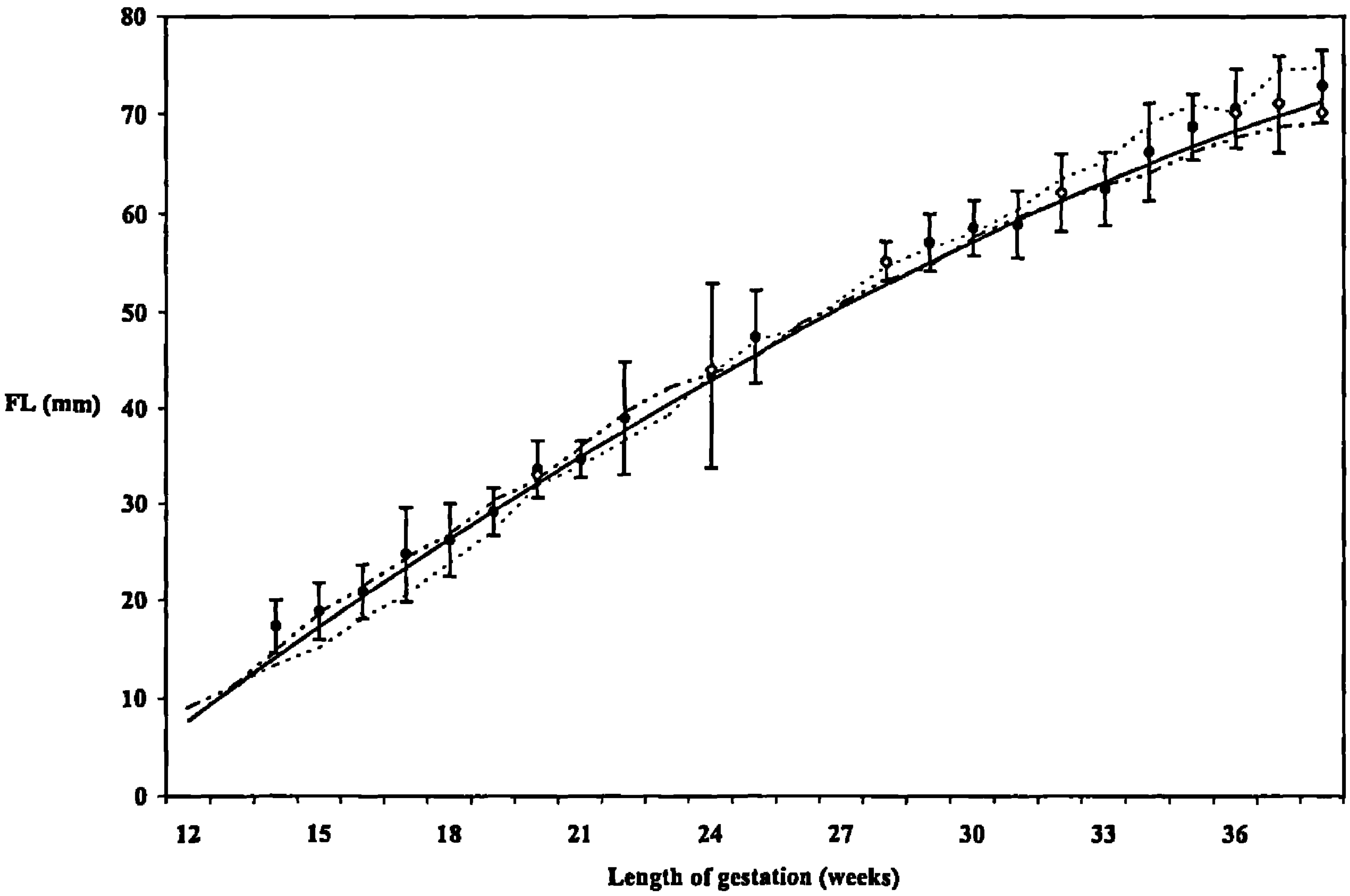

Fig. 2. Femur length (FL; mm) for week of gestation compared with FL measurements from England [16] (solid line), Australia [18] (line and dash), Papua New Guinea [2] (dashed line), and India [4] (◇). Data for Guatemalan sample (●; mean ± S.D.) are shown when $n > 5$.

document how early fetal growth faltering may influence gestational age estimation based on ultrasound.

Considering that the Guatemalan infants in this study were born small on average compared to the reference, we expected that this would be reflected in the ultrasound measurements from that point in gestation when growth restriction begins. BPD and HC confirm our expectations in that they do indicate growth restriction, evident at 30 weeks' gestation. Contrary to our expectations, FL and AC do not conform to the pattern of growth restriction. Both dimensions closely follow to the reference mean throughout gestation. At this time, we have no adequate explanation of these findings. Mean length at birth in this population is 1 S.D. below the reference of length for gestational age, and the entire distribution of birth length is shifted, suggesting that linear growth of long bones must have been compromised during gestation. Although the description of measurement techniques for FL and AC is similar between the reference and our study, slight systematic differences in technique may explain these finding. Standard deviations for all ultrasound measures in the current series tend to be slightly higher than those reported in the literature, particularly in mid-gestation. This may be due to small sample size at some gestational ages or may reflect increased variability due to fetal growth restriction. Considering that our ultrasonographers were highly trained and underwent a standardization exercise to ensure appropriate measurement techniques, we do not believe that the higher S.D. is related to greater measurement error. Other studies from developing countries have reported data for ultra-

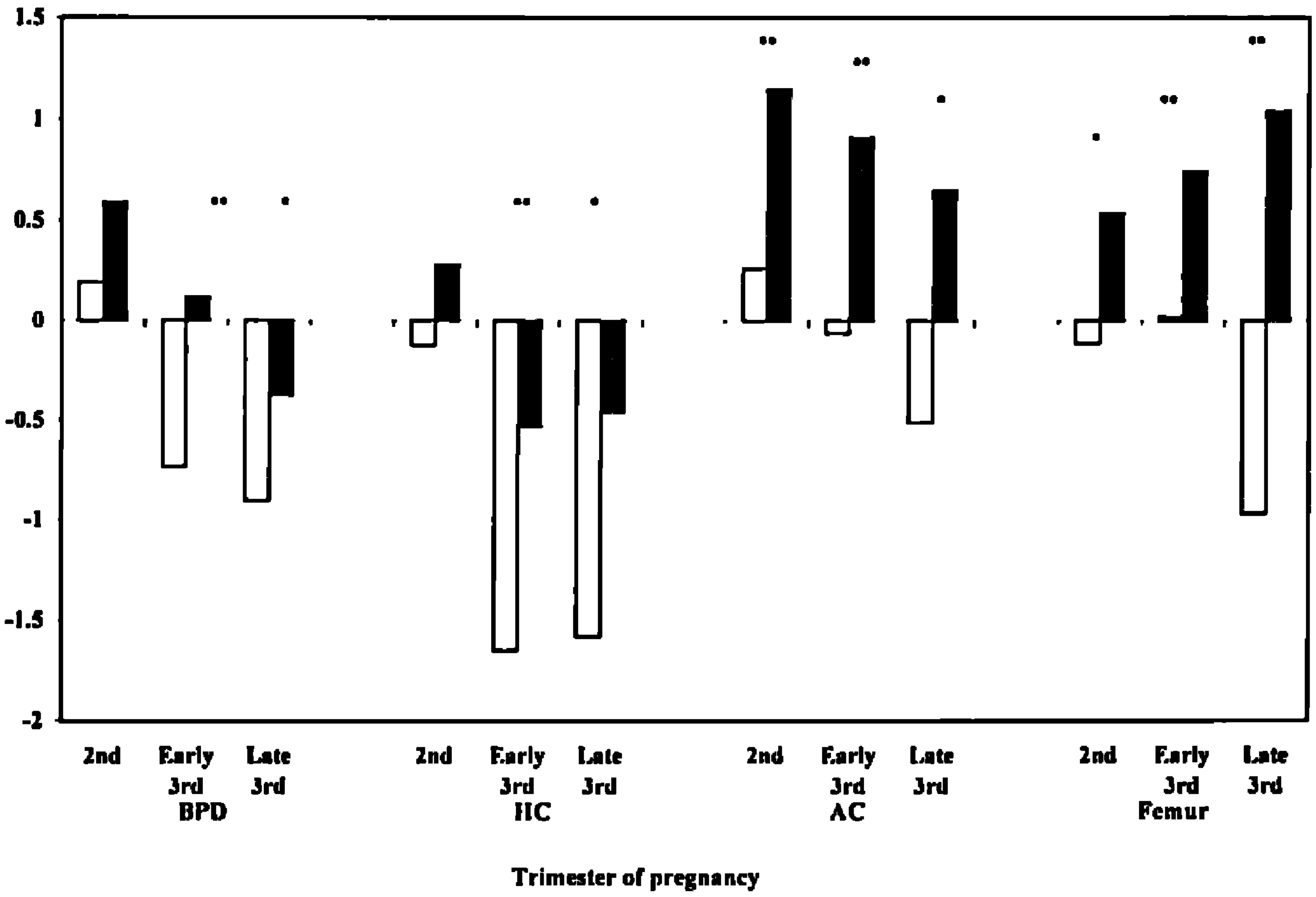

Fig. 3. Mean ultrasound Z scores for biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC) and femur length during the 2nd trimester (15–18 weeks' gestation), early 3rd trimester (28–32 weeks), and late 3rd trimester (35–38 weeks) for infants with (□) and without (■) low weight for gestational age at birth. $^{*}P<0.05$; $^{**}P<0.01$.

sound measurements which are inconsistent with their small mean birth size (see e.g. FL from Papua New Guinea and India; Fig. 2). Until studies that assure similar technique in developed and developing countries are conducted, it is difficult to make conclusions regarding the differences in fetal size between developing country measurements and developed country references.

The comparison of ultrasound measurements of Guatemalan infants born SGA and non-SGA avoids potential errors due to differences in measurement technique between our study and published references. By 15 weeks' gestation, FL and AC are significantly smaller among SGA infants. Although the differences did not reach statistical significance, a similar pattern is evident in BPD and HC. Contrary to the conclusions made when our results are compared with reference values, the comparison between SGA and non-SGA infants suggests that growth faltering begins early in gestation and affects all dimensions of fetal size.

Small BPD in the second trimester may have important implications for the estimation of gestational age based on ultrasound in this population. The BPD of infants eventually born SGA is approximately 0.3 standard deviations or 0.75 mm at 15–18 weeks' gestation compared with non-SGA infants. Considering that the growth rate of BPD from 16 to 19 weeks' gestation is approximately 3.08 mm/week [19], this difference would translate into 2–3 days of gestational age. This could bias the estimation of gestational age using BPD in populations such as Guatemala. However, in our sample, there was no difference between SGA and non-SGA newborns in BPD-based gestational age implying that the smaller BPD among SGA infants during the early second trimester was not large enough to influence gestational age estimation.

One strength of this study is that our gestational age estimation is independent of fetal size. In rural areas of developing countries, it is common for women to be unsure of LMP date and to present for prenatal care late in pregnancy resulting in large errors in gestational age estimation. Because this was a large longitudinal study with training to ensure high quality information regarding LMP, and early identification of pregnancies, LMP dates are probably more accurate than generally possible.

The women who participated in the current study are marginally malnourished as evidenced by short maternal height (mean = 149 cm) and low total weight gain during pregnancy (mean = 8 kg). When nutritional status during early childhood was improved in this population through nutritional supplementation, linear growth improved [20], as did birth size in the subsequent generation [21]. This suggests that nutrition is a limiting factor for growth both pre- and postnatally and that the high prevalence of SGA may reflect a high prevalence of IUGR related to maternal nutritional deficiency. In this study, we found that infants who were eventually born SGA were smaller in all ultrasound measurements beginning as early as 15 weeks' gestation. An association between small fetal size in the first trimester and higher risk of low birth weight has previously been reported in a population from the UK [22]. This may have important implications for the timing of interventions to improve fetal growth in marginally malnourished populations. A strong relationship has been found between maternal anthropometry during different stages of pregnancy and infant birth weight and recumbent length [23]. The relationship between maternal past and current nutritional status, with an emphasis on pre- and early pregnancy and its relation to fetal growth in both early and late gestation needs to be established.

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