

The Thin But Fat Phenotype is Uncommon at Birth in Indian Babies

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ABSTRACT

Background: Indian babies are hypothesized to be born thin but fat. This has not been confirmed with precise measurements at birth. If it is true, it could track into later life and confer risk of noncommunicable diseases (NCDs).

Objectives: Primarily, to accurately measure percentage of body fat (%BF) and body cell mass (BCM) in Indian babies with normal birth weight, compare them across different gestational ages and sex, and test the hypothesis of the thin but fat phenotype in Indian babies. Secondly, to examine the relation between body weight and body fat in Indian babies.

Methods: Term newborns ($n = 156$) weighing ≥ 2500 g, from middle socioeconomic status mothers were recruited in Bengaluru, India, and their anthropometry, %BF (air displacement plethysmography), and BCM (whole-body potassium counter) were measured. Maternal demography and anthropometry were recorded. The mean %BF and its dispersion were compared with earlier studies. The relation between newborn %BF and body weight was explored by regression analysis.

Results: Mean birth weight was 3.0 ± 0.3 kg, with mean %BF $9.8 \pm 3.5\%$, which was comparable to pooled estimates of %BF from published studies (9.8%; 95% CI: 9.7, 10.0; $P > 0.05$). Appropriate-for-gestational age (AGA) babies had higher %BF (1.8%) compared to small-for-gestational age (SGA) babies ($P < 0.01$). Mean %BCM of all babies at birth was $35.4 \pm 10.5\%$; AGA babies had higher %BCM compared to SGA babies (7.0%, $P < 0.05$). Girls in comparison to boys had significantly higher %BF and lower %BCM. Body weight was positively associated with %BF.

Conclusion: Indian babies with normal birth weight did not demonstrate the thin but fat phenotype. Body weight and fat had positive correlation, such that SGA babies did not show a preservation of their %BF. These findings will have relevance in planning optimal interventions during early childhood to prevent NCDs risk in adult life. *J Nutr* 2020;150:826–832.

Keywords: Indian newborns, thin fat phenotype, air displacement plethysmography, percentage of body fat, body cell mass

Introduction

South Asian children have been observed to have more fat for a given BMI when compared to Caucasians (1, 2). This relative fatness has been extended to fetal growth as well, based on a report that Indian babies appeared to have preserved subscapular skinfold thickness at birth in comparison with UK babies, even though they had lower birth weights (3). It has been proposed that the accretion of body fat (BF) is preserved relative to the faltering of fetal growth in an adverse uterine environment (or as a result of intergenerational effects) (4–6), resulting in the proposed phenotype of a thin but fat Indian

or South Asian newborn. The fetal programming hypothesis suggests that environmental conditions during fetal and early infancy affect long-term health and capacity through permanent effects on growth, structure, and metabolism. The structural and physiological changes that occur in response to impaired fetal growth may reduce growth and lower birth weight, with the programmed fetus being at risk of developing chronic diseases in adult life (5, 7). It should, however, be noted that early life programming can occur even in the absence of changes in the birth weight (8). Early life adiposity can track into later life and could relate to adult risk for noncommunicable diseases (NCDs) (7). The measurement of body composition

in newborns is therefore particularly relevant in India, a low-to middle-income country where there has been an explosive growth of the prevalence of adult NCDs (9–11), and where urgent population-level health measures need to be taken.

Although human babies are born with more fat (primarily subcutaneous) than other mammals with precocial newborns (12), their body water content is about 80%, with more extracellular water than intracellular water; approximately 45% and 35% of the body weight, respectively (13). This relatively higher water content in the newborn, does not leave much space in the body for the other (dry) components, of fat-free mass (FFM) and fat mass (FM), to increase. The thin but fat hypothesis of Indian babies was primarily based on measurements of the subscapular skinfold thickness of newborns; this finding, however, was subsequently not replicated in India (14, 15). An earlier study using whole-body magnetic resonance imaging, found no difference in the whole-body adipose tissue between Indian and white European babies (measured in the second week of life), but reported that the Indian neonates had significantly higher superficial subcutaneous, deep subcutaneous, and visceral adipose tissue (16). Similarly, later measurements of the BF by deuterium dilution, of Indian neonates about 12 d after birth found a fat content of 11.3%, which was similar to other neonate populations (17). These suggest that the generalization of the thin but fat phenotype in Indian babies at birth is questionable, and accurate methods of body composition in newborns, measured as soon as possible after birth are needed, because rapid changes occur in body composition, particularly during the first week of life (18).

Body fat in newborns can be accurately measured using an infant air displacement plethysmograph, which measures body volume, from which body density and the proportion of BF can be calculated (18). The infant air displacement plethysmograph (PEA POD) has also been shown to be relatively robust to small changes in the hydration of FFM (19). The important metabolic component of the FFM, the body cell mass (BCM), can be measured from the whole-body potassium content (20) and is, importantly, independent of changes in the extracellular water. Differential responses to maternal diet in the fetus, dependent on sex, have been recently reported (21), and thus exploring the impact of sexual dimorphism on body composition of newborns would be an interesting facet. The primary objective of the study was to accurately measure the BF and BCM of Indian newborns, within 3–5 d of birth, to compare them across the different levels of gestational age and sex and to test the hypothesis of the thin but fat phenotype in normal birth weight Indian babies. The secondary objective was to examine the relation between body weight and BF in these newborns to evaluate the putative preservation of BF deposition in the face of lower intrauterine growth.

Methods

Full-term (≥ 37 weeks of gestation) newborns weighing ≥ 2500 g delivered between September 2017 and January 2019 at St. John's Medical College Hospital, Bengaluru, a tertiary care hospital in a cosmopolitan city catering to patients of all strata, from all over the country, were screened for their eligibility. All the women delivering in the obstetric ward were approached for the study and the infants were recruited based on the inclusion/exclusion criteria and parental consent. All infants weighing ≥ 2500 g, from singleton pregnancies of healthy mothers were recruited. The modified Kuppaswamy scale, which captured details on occupation, education, and income of the family (22), was used to categorize socioeconomic status; the women of the present study belonged to the middle socioeconomic stratum. A purposive sampling design was used at birth, to include healthy neonates, whereas neonates with congenital abnormalities or other birth defects were excluded. A total of 156 newborns were enrolled, after obtaining informed written parental consent. Details of subject screening and enrolment are provided in **Supplemental Figure 1**. The study was approved by the Institutional Ethical Review Board of St. John's Medical College Hospital. In 64.7% of the newborns, body composition measurements were made within 0–72 h of birth. Maternal demography, anthropometry, obstetric history, and education were recorded. Postpartum maternal height was measured to the nearest 0.1 cm using a portable stadiometer (SECA 213). The pre-pregnant or first trimester weight of the mothers was taken from hospital records where available. The third trimester weight, which was measured at the end of the third trimester when the mother was admitted for the delivery of the baby, was obtained from the hospital records. Gestational weight gain (kg) was calculated as the difference between the weights at the third and first trimesters.

Newborn length was measured to the nearest 0.1 cm using an infantometer (SECA 417). Body weight on the day of measurement was measured to the nearest 0.01 kg using a baby scale (Salter 914). Head circumference was measured to the nearest 0.1 cm using a measuring tape (ADC 396). The measurements were performed by 2 trained nutritionists. To measure the interobserver differences, each nutritionist performed the anthropometric measurements on 10 babies, while for intraobserver difference, the nutritionists measured a baby 10 times each. The interobserver and intraobserver differences for the anthropometric measurements were calculated and observed to be $\leq 0.1\%$. Body composition of the newborn was measured by air displacement plethysmograph (PEA POD, Software version 3.5.0, 201, COSMED USA) with standard procedures (23). The air displacement plethysmograph was calibrated daily, with a hollow cylinder of known mass and volume, and had a measurement precision of 0.07% (**Supplemental Methods**). Total body density was calculated as the ratio of weight (kg) and the measured body volume (L) and used to calculate the proportions of FM and FFM using assumed densities (0.9007 and 1.063 kg/L for FM and FFM, respectively). The FM and FFM were also expressed as a percentage of body weight (%BF; %FFM).

The total body potassium (TBK) of the newborns was measured from the naturally occurring radioactive isotope (^{40}K), using a whole-body potassium counter (WBKC) with a shadow shield design (20). The characteristic high-energy γ rays (1461 keV) of ^{40}K from the neonates were measured in a 60-min period, during which the neonates were swaddled in a blanket and placed in a plastic bassinet directly underneath the detectors, in the center of the WBKC. A unique feature of the aperture in the design of the WBKC allowed neonates to be counted in static geometry, at maximum sensitivity, within direct vision of a parent or trained operator (20). A Conseil Européen pour la Recherche Nucléaire ROOT package (24) was used to analyze the count data of ^{40}K , scaled to the time interval of the measurement. The ^{40}K counts (counts per second, CPS) relation to the TBK was also defined to calibrate the WBKC for measurement of small babies. Anthropomorphic dummies or phantoms with different weights and known amounts of K were used for the calibration. This included 4 phantoms, weighing 0.95, 2.08, 3.20, and 5.25 kg, with a constant height of 50 cm and 3 phantoms, weighing 7.91, 9.90, and 12.94 kg, with a constant height of 80 cm, prepared with known quantities

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Supplemental Figure 1 and Supplemental Methods with details on precision, accuracy, and mean counting error are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at <https://academic.oup.com/ijn>.

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Abbreviations used: AGA, appropriate-for-gestational age; BCM, body cell mass; BF, body fat; CPS, counts per second; FFM, fat-free mass; FM, fat mass; LGA, large-for-gestational age; NCDs, noncommunicable diseases; SGA, small-for-gestational age; TBK, total body potassium; WBKC, whole-body potassium counter.

of potassium chloride (KCl). Combinations of plastic containers of different sizes were used to simulate the head, arms, trunk, and legs of the phantoms. The head of the 50 cm phantoms was 0.86 kg in weight and 13 cm in length, while the head of the 80 cm phantoms was 2.00 kg in weight and 17 cm in length. The proportions of the limbs and trunk of the phantoms were adjusted to ensure that the surface area to body weight ratio corresponded to that of a baby with similar weight and length, calculated by the Meban formula for body surface area (25, 26). Deionized water phantoms equivalent to the weight and shape of the corresponding KCl phantoms were also constructed and scanned under the WBKC. Detector-specific water phantom CPS were subtracted from the KCl phantom CPS to get net CPS. Monte Carlo calculations were then applied to the different phantom geometries to simulate neonates of different shapes and sizes (27). The precision and mean counting error of the WBKC were calculated by measuring each phantom 12 times. The mean counting error for the neonates was also calculated. The accuracy of the WBKC for a very small baby was calculated using a phantom which was not a part of the calibration series. The test phantom (1.13 kg weight and 50 cm length) containing 120.36 g K was measured overnight for 12 h in the same manner as the other phantoms. Based on the net CPS obtained for the test phantom, K was estimated to be 122.28 g, which gave an accuracy error of -1.59% and an accuracy of 98.41% . The mean precision of the instrument was found to be 0.4% of TBK and the mean counting error ranged from 0.16% to 0.69% for the different phantoms. The mean counting error for the 156 neonates was found to be $10.0 \pm 3.5\%$ (Supplemental Methods). Because the BCM contains 98% of TBK under tight homeostatic control, unaffected by the hydration status of the body, a near constant ratio of TBK to BCM ($108.7 \text{ mmol K/kg BCM}$), invariant across age and sex, was used to calculate BCM from TBK (28). The BCM was also expressed as a percentage of body weight (%BCM).

To externally evaluate the measurements made in this study, an extensive literature review was conducted using the PubMed search engine to capture global data on body composition estimates of babies at birth. Search terms arranged along with boolean operators in the following fashion [((((Body Composition(Text Word)) AND newborn(Text Word)) OR neonate(Text Word)) OR infant(Text Word)) NOT preterm(Text Word)) NOT child*(Text Word)) AND plethysmography(Text Word)] resulted in a find of 72 studies after filters relating to species (humans), age (birth to 1 mo) and date of publication between January 2013 to December 2018 had been applied. All 72 studies were screened for their eligibility, wherein titles of 16 studies and abstracts of 9 studies did not yield any information relevant to the topic of interest. The remainder articles were subjected to a thorough analysis to find studies that met the criteria. Of the 47 remaining studies, 7 had measured the body composition estimates at postnatal age $>5 \text{ d}$, while 12 studies did not provide adequate information. In another 12, multiple studies reported the same body composition estimates from the same cohorts and thus only the primordial/largest studies among them were considered. Thus, a total of 16 articles (4, 29–44) from the 72 were included in the final analysis. A prominent study from 2011 (35) was also included, however, as it had a large sample size and a robust study design. Thus, 17 studies meeting the criteria of exclusively using the air displacement plethysmograph technique for body composition measurements within 5 d of birth were included to create a comparative analysis for estimates of %BF obtained from the present study.

Data are presented as means \pm SDs for quantitative parameters such as anthropometric and body composition estimates, while frequency and percentage (%) were used for qualitative parameters such as education and parity. The neonates were classified as small-for-gestational age (SGA), large-for-gestational age (LGA), and appropriate-for-gestational age (AGA) using the INTERGROWTH newborn size standards (45); with SGA, being defined as $<10\text{th}$ centile of birth weight for gestational age, LGA, being defined as $>90\text{th}$ centile of birth weight for gestational age and AGA, being defined as between the 10th and 90th centiles of birth weight for gestational age (46). The different measured characteristics of the babies were compared across the different levels of gestational age (AGA, SGA) and sex by independent *t* test. The pooled mean estimate of %BF was obtained by weighted average of all the mean values of %BF from different

TABLE 1 Description of maternal characteristics of the newborns¹

Variables	Values
Age, y	26.0 \pm 4.5
Gestational age, wk	38.9 \pm 1.0
Pre-pregnant or first trimester weight, ² kg	54.7 \pm 10.1
Height, ³ cm	155.8 \pm 5.7
Pre-pregnancy BMI, ⁴ kg/m ²	22.4 \pm 4.2
Third trimester weight, ⁵ kg	66.9 \pm 10.9
Gestational weight gain, ⁶ kg	12.0 \pm 4.4
Maternal educational status	
Attended primary school, %	22.4
Attended secondary school, %	28.2
Completed Bachelor's degree, %	37.2
Completed Master's degree, %	12.2
Parity	
Primiparous, %	65.2
Multiparous, %	34.8

¹Values are presented as means \pm SDs or as percentages, $n = 156$ unless stated otherwise.

²Pre-pregnant or first trimester weight, obtained from the hospital records, was measured within ≤ 12 wk of gestational age, $n = 155$.

³Postpartum height, $n = 155$.

⁴ $n = 154$.

⁵The third trimester weight, obtained from the hospital records was measured at the end of the third trimester when the mother was admitted for the delivery of the baby, $n = 145$.

⁶Gestational weight gain was calculated as the difference between third and first trimester body weights, $n = 145$.

studies (as mentioned above), with the weight being the sample size of different studies. The pooled SD was also obtained by the same method to estimate the 95% CI. The pooled mean estimate of %BF and its 95% CI were compared with the estimates of the present study by a forest plot. Significant overlap between 95% CI of the pooled and study estimates was considered as the criteria for testing the hypothesis. Further confirmation of this visual impression was performed using Student's two-sample test for equal means. The relation between %BF and body weight of neonates was explored by scatter plot and regression technique. The data were analyzed by statistical software R version 3.5.3 (47) and *P* values < 0.05 were considered statistically significant.

Results

The mean age of the participating mothers was $26.0 \pm 4.5 \text{ y}$ and their mean height was $155.8 \pm 5.7 \text{ cm}$ (Table 1). About half the mothers had graduate or higher education, and none of them were illiterate. Almost two-thirds of the mothers were primiparous. The mean birth weight of the 156 neonates (equal distribution by sex) was $3.0 \pm 0.3 \text{ kg}$. Of these, 19 (12.2%) neonates were SGA with a mean birth weight of $2.7 \pm 0.1 \text{ kg}$. The mean age of 156 neonates on the day of measurement was $2.8 \pm 1.4 \text{ d}$; wherein 20.5% of babies were measured within 24 h of birth, and the remaining 19.9%, 24.4%, 23.1%, and 12.2% were measured within 48, 72, 96, or 120 h of birth, respectively.

The mean %BF for the whole group measured by air displacement plethysmograph was $9.8 \pm 3.5\%$ (Table 2). The %BF of the AGA babies was significantly higher (by 1.8%; $P < 0.01$) when compared to the SGA babies. The girls had a significantly higher %BF (by 1.1%; $P < 0.05$) when compared to the boys. The mean %BCM of the whole group at birth was $35.4 \pm 10.5\%$. The AGA babies had a significantly higher %BCM (by 7.0%; $P < 0.05$) than the SGA babies, and the boys

TABLE 2 Distribution of body composition and characteristics of term neonates at birth, stratified by gestational age and sex¹

Variables	Whole group (n = 156)	Segregation according to gestational age			Segregation according to sex		
		AGA (n = 134)	SGA (n = 19)	P value	Male (n = 73)	Female (n = 83)	P value
Gestational age, d	272.0 ± 6.7	271.3 ± 6.5	276.8 ± 6.2	0.001	271.7 ± 6.8	272.3 ± 6.7	0.566
Age, ² d	2.8 ± 1.4	2.8 ± 1.4	3.0 ± 1.7	0.607	2.9 ± 1.5	2.7 ± 1.3	0.356
Length, cm	48.2 ± 1.7	48.3 ± 1.7	47.0 ± 0.9	<0.001	48.7 ± 1.8	47.8 ± 1.5	0.001
Birth weight, kg	3.0 ± 0.3	3.0 ± 0.3	2.7 ± 0.1	<0.001	3.1 ± 0.3	3.0 ± 0.3	0.092
Body weight, ² kg	2.8 ± 0.3	2.8 ± 0.3	2.5 ± 0.1	<0.001	2.9 ± 0.3	2.8 ± 0.3	0.044
Delta weight, ³ kg	0.20 ± 0.10 ⁴	0.21 ± 0.09 ⁴	0.14 ± 0.08 ⁴	0.008	0.20 ± 0.10 ⁴	0.20 ± 0.09 ⁴	0.628
Head circumference, ⁵ cm	33.3 ± 1.1	33.3 ± 1.1	33.0 ± 0.8	0.101	33.8 ± 1.0	32.9 ± 1.0	<0.001
FM, kg	0.3 ± 0.1	0.3 ± 0.1	0.2 ± 0.1	<0.001	0.268 ± 0.111 ⁴	0.289 ± 0.119 ⁴	0.257
FM, %	9.8 ± 3.5	9.9 ± 3.5	8.1 ± 2.4	0.007	9.2 ± 3.2	10.3 ± 3.7	0.043
FFM, kg	2.5 ± 0.2	2.5 ± 0.2	2.3 ± 0.1	<0.001	2.6 ± 0.2	2.5 ± 0.2	0.002
BCM, kg	1.0 ± 0.3	1.0 ± 0.3	0.7 ± 0.3	<0.001	1.1 ± 0.3	0.9 ± 0.3	0.018
BCM, %	35.4 ± 10.5	36.2 ± 10.2	29.2 ± 10.5	0.012	37.3 ± 10.6	33.8 ± 10.2	0.036
TBK, g	4.3 ± 1.4	4.4 ± 1.4	3.1 ± 1.1	<0.001	4.5 ± 1.4	4.0 ± 1.4	0.018

¹Values are presented as means ± SDs. AGA, appropriate-for-gestational age, defined as between the 10th and 90th centiles of birth weight for gestational age (45); BCM, body cell mass; FFM, fat-free mass; FM, fat mass; SGA, small-for-gestational age, defined as <10th centile of birth weight for gestational age (45); TBK, total body potassium.

²Taken on day of measurement.

³Delta weight was calculated for each neonate as the difference between birth weight and weight on the day of the measurement.

⁴Values have been presented up to 2 or more decimal places to provide clarity and avoid confusion associated with truncation.

⁵n = 155 for head circumference measurement under the whole group category.

had an approximately 3.5% significantly higher value than the girls. These details are summarized in Table 2.

Figure 1 presents the forest plot of estimates of %BF obtained from different studies through the literature review, along with the estimates from the present study. The mean %BF varied from 7.3 ± 4.6% (34) to 11.4 ± 4.1% (39) for the data obtained from the systematic search. The pooled estimate of %BF was 9.8 ± 0.3% (95% CI: 9.7, 10.0) while the mean %BF from the present study was 9.8 ± 3.5%. The Student's *t* test for equal mean, failed to reject the null hypothesis (*P* > 0.05).

The %BF of the neonates was positively associated with body weight (Figure 2). An increase of 3.5 units with 95% CI: 3.3, 3.7; *P* < 0.05 in %BF was observed for every 1 kg increase in body weight in boys, while the increase was 3.2 units in %; 95% CI: 3.0, 3.4; *P* < 0.05 for girls.

Discussion

The present study, the first of its kind in India used an accurate and validated measurement (air displacement plethysmograph) of body composition in Indian newborns (19), to show that they had %BF similar to estimates obtained in other populations. The mean %BF of the Indian newborns was similar and within the 95% CI, of the pooled estimate of %BF (9.8%) measured by air displacement plethysmograph in different populations (Figure 1), whose mean birth weight was 3.3 ± 0.1 kg, and somewhat higher than the present study (3.0 ± 0.3 kg).

The thin but fat phenotype described in Indian neonates was based on comparative anthropometric measurements in newborns born in Pune, a city in West India and Southampton, UK (3). Anthropometric measurements are, however, sometimes limited by their precision and accuracy (15, 18). It is also important to note that the pregnant women from both Indian studies differed in time, location, wealth, educational status, and (perhaps) nutritional status. The women of the Pune study were poorly educated, rural women, while women from the present study were educated, 50% had a graduate degree or higher and none were illiterate. The mothers from the Pune study also had

a lower pre-pregnancy weight (by 13.0 kg), were shorter (by 3.8 cm), and had a lower BMI (by 4.2 kg/m²) when compared to the women from the present study. Although findings similar to the Pune cohort were found in another newborn cohort from the South Indian city of Mysore (1), these findings were not replicated in newborn studies from other South Indian cities of Bengaluru (14) and Hyderabad (48). Thus, it is not clear whether ethnicity, maternal phenotype, or the local environment may play a significant influence on the newborn FM. The results of the current study are credible, however, because the method of body composition used for the neonates was accurate and precise. The findings were also similar to another study (17), which used an equally accurate method of deuterium dilution and found the %BF (11.3%) at age 2 wk, to be comparable to that of babies of similar age from Western populations. Thus, comparative analyses of findings from this paper with the literature findings, does lead to rejection of the hypothesis of the “thin but fat” phenotype at birth in Indian babies.

In addition, in the present study, there was a significant positive correlation between body weight and %BF across the weight range of 2.3–3.6 kg (Figure 2). Similar results were observed earlier in North Indian newborns with birth weight ranging from 2 to 4 kg, where %BF, was measured by deuterium dilution (17). Ethiopian infants measured at birth using air displacement plethysmography, showed similar findings, with no relative preservation of fat at the expense of the FFM; however, this did occur in girls during early postnatal growth, rather than fetal life (35). The size for gestational age at birth is another important variable that could affect fetal body composition, and it might also be hypothesized that the postulated fat-sparing effect might be more relevant to SGA or preterm babies. However, term SGA neonates have been shown to have a lower %BF compared to AGA neonates (49, 50), and SGA babies from the present study demonstrated a similar pattern, with both %BF and %BCM being significantly lower in comparison to the AGA neonates, the latter implying that SGA infants could have a lower proportion of skeletal muscle mass. Further, the Intergrowth-21st study also observed that the lower birth weight of either preterm or SGA babies was associated with lower FM and FFM in comparison to AGA babies (33).

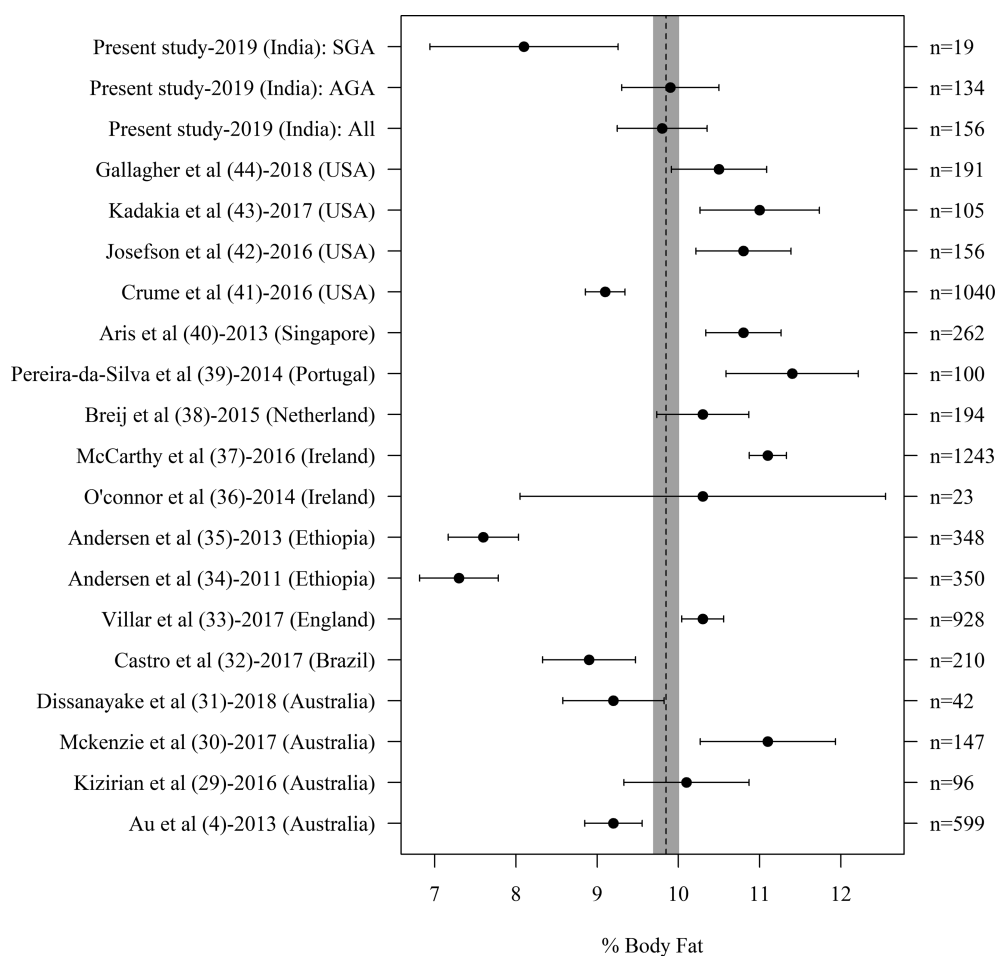


FIGURE 1 Comparison of %BF of newborns measured by air displacement plethysmography from the present study with studies having similar measurements across different populations, over the last 8 y (2011–2018). The %BF of newborns from the present study segregated by gestational age as SGA, defined as <10th centile of birth weight for gestational age, and AGA, defined as between the 10th and 90th centiles of birth weight for gestational age (46), has also been presented for comparative analysis. The vertical dotted line with shaded CI band is the pooled mean %BF (9.8; 95% CI: 9.7, 10.0) obtained from different published studies. AGA, appropriate-for-gestational age; %BF, percentage of body fat; SGA, small-for-gestational age.

These findings do not support the previously suggested BF-conserving hypothesis in smaller babies from West India (3) for a general phenotype of thin but fat, although the sample size of the SGA babies in the present study was small. More studies with a larger sample size on SGA babies are needed to confirm the findings of the present study.

The present study also provides new data relating to the newborn FFM (through BCM estimates) at birth. Fetal FFM has been shown to track into childhood (4 y) in an Ethiopian cohort of children (51), and positively predicted height (52), cognitive development at 2 y (53), and linear growth from age 1 to 5 y (51). The measurement of BCM, the metabolically active tissue, is accurate because the hydration and extracellular fluid volume of the FFM is higher and variable in newborns as they progress through the first days of life. The BCM measurement is independent of the extracellular fluid, and in the present study was about 35% of body weight, which was comparable to BCM estimates made in US neonates, albeit measured 2 wk after birth (54). It remains to be seen, however, whether the BCM estimates would be similar in babies born to mothers in poverty, with poor nutritional status.

Differences in body composition by sex have been observed in earlier studies (34, 55). In the present study, boys had a higher %FFM and %BCM, whereas girls had a significantly

higher %BF. Data from the Intergrowth-21st study suggests that boys had higher FFM when compared to girls after 34 weeks of gestation, with lower FM at birth (33). Sex-specific placental, hormonal, and maternal anthropometric influences, and many unknown factors could interact in many complex ways affecting fetal growth and body composition. Fetal sex-specific association of maternal diet with placental expression of angiogenic genes has been recently reported (21). Insulin-like growth factor-1, the main growth-promoting factor during intrauterine life has been observed to be higher in girls than boys at birth, along with higher levels of insulin-like growth factor binding protein-3 (56, 57); however, the biological significance is unknown. Thus, although there is evidence for the sexual dimorphism in body composition at birth, more studies are needed to elucidate causal relations between its hypothesized determinants and body compositional outcomes at birth, as well as their consequences on health and disease in later life.

A limitation of the present study was that it was purposively carried out in newborns, born to healthy middle-class mothers from South India. There is, however, no evidence to suggest that babies born elsewhere in India belonging to different regional ethnicities would be different. In addition, families from all regions of India reside in Bengaluru. The possible effects of differences in nutritional status and health on the findings of

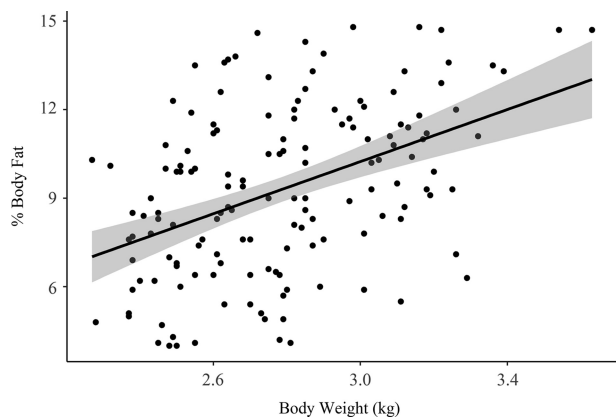


FIGURE 2 Scatter plot showing the linear relation between body weight and %BF measured by air displacement plethysmography. The straight line and the shaded portion depict the regression line with 95% confidence band of %BF on body weight. %BF, percentage of body fat.

the present study are not known and whether these findings will be similar in babies born to undernourished mothers, or in low birth weight/preterm newborns needs to be explored. In conclusion, this study presents data for the first time on the body composition of Indian neonates using accurate air displacement plethysmograph and WBKC measurements. The findings of this study suggest that the thin but fat phenotype does not exist in Indian babies born to healthy mothers. In addition, babies born SGA also do not appear to have a preserved, or higher, %BF. The previously observed findings of putative thin but fat phenotype thus may not necessarily apply to all Indian newborns.

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References

1. Krishnaveni GV, Hill JC, Veena SR, Leary SD, Saperia J, Chachyamma KJ, Karat SC, Fall CHD. Truncal adiposity is present at birth and in early childhood in South Indian children. *Indian Pediatr* 2005;42: 527–38.
2. Lakshmi S, Metcalf B, Joglekar C, Yajnik CS, Fall CH, Wilkin TJ. Differences in body composition and metabolic status between white U.K. and Asian Indian children (EarlyBird 24 and the Pune Maternal Nutrition Study). *Pediatr Obes* 2012;7:347–54.
3. Yajnik CS, Fall CHD, Coyaji KJ, Hirve SS, Rao S, Barker DJP, Joglekar C, Kellingray S. Neonatal anthropometry: the thin-fat Indian baby. The Pune Maternal Nutrition Study. *Int J Obes Relat Metab Disord* 2003;27:173–80.
4. Au CP, Raynes-Greenow CH, Turner RM, Carberry AE, Jeffery H. Fetal and maternal factors associated with neonatal adiposity as measured by air displacement plethysmography: a large cross-sectional study. *Early Hum Dev* 2013;89:839–43.
5. Gluckman PD, Hanson MA, Cooper C, Thornburg KL. Effect of in utero and early-life conditions on adult health and disease. *N Engl J Med* 2008;359:61–73.

6. Hemachandra AH, Klebanoff MA. Use of serial ultrasound to identify periods of fetal growth restriction in relation to neonatal anthropometry. *Am J Hum Biol* 2006;18:791–7.
7. Haire-Joshu D, Tabak R. Preventing obesity across generations: evidence for early life intervention. *Annu Rev Public Health* 2016;37:253–71.
8. Fall CHD. Fetal programming and the risk of noncommunicable disease. *Indian J Pediatr* 2013;80:13–20.
9. Arokiasamy P. India's escalating burden of non-communicable diseases. *Lancet Glob Health* 2018;6:e1262–3.
10. Nethan S, Sinha D, Mehrotra R. Non communicable disease risk factors and their trends in India. *Asian Pac J Cancer Prev* 2017;18:2005–10.
11. World Health Organization. Global status report on noncommunicable diseases. Geneva, Switzerland; 2014.
12. Kuzawa CW. Adipose tissue in human infancy and childhood: an evolutionary perspective. *Am J Phys Anthropol* 1998;Suppl 27:177–209.
13. Friis-Hansen B. Body water compartments in children: changes during growth and related changes in body composition. *Pediatrics* 1961;28:169–81.
14. Muthayya S, Dwarkanath P, Thomas T, Vaz M, Mhaskar A, Mhaskar R, Thomas A, Bhat S, Kurpad A. Anthropometry and body composition of south Indian babies at birth. *Public Health Nutr* 2006;9:896–903.
15. Kulkarni B, Mamidi RS, Balakrishna N, Radhakrishna KV. Body composition assessment in infancy and early childhood: comparison of anthropometry with dual-energy X-ray absorptiometry in low-income group children from India. *Eur J Clin Nutr* 2014;68:658–63.
16. Modi N, Thomas EL, Uthaya SN, Umrani S, Bell JD, Yajnik C. Whole body magnetic resonance imaging of healthy newborn infants demonstrates increased central adiposity in Asian Indians. *Pediatr Res* 2009;65:584–7.
17. Jain V, Kurpad AV, Kumar B, Devi S, Sreenivas V, Paul VK. Body composition of term healthy Indian newborns. *Eur J Clin Nutr* 2016;70:488–93.
18. Demerath EW, Fields DA. Body composition assessment in the infant. *Am J Hum Biol* 2014;26:291–304.
19. Ellis KJ, Yao M, Shypailo RJ, Urlando A, Wong WW, Heird WC. Body-composition assessment in infancy: air-displacement plethysmography compared with a reference 4-compartment model. *Am J Clin Nutr* 2007;85:90–5.
20. Naqvi S, Bhat K, Preston T, Devi S, Joseph J, Sachdev H, Kurpad AV, Kuriyan R. The development of a whole-body potassium counter for the measurement of body cell mass in adult humans. *Asia Pac J Clin Nutr* 2018;27:1190–7.
21. Mani C, Kochhar P, Ravikumar G, Dwarkanath P, Sheela CN, George S, Thomas A, Crasta J, Thomas T, Kurpad AV, et al. Placental expression of ENG, VEGF, and FLT: gender-specific associations with maternal vitamin B12 status. *Eur J Clin Nutr* 2019; doi: 10.1038/s41430-019-0449-2. [Epub ahead of print].
22. Saleem DSM. Modified Kuppuswamy scale updated for year 2018. *Paripex Indian J Res* 2018;7:435–6.
23. Urlando A, Dempster P, Aitkens S. A new air displacement plethysmograph for the measurement of body composition in infants. *Pediatr Res* 2003;53:486–92.
24. Conseil Européen pour la Recherche Nucléaire. ROOT data analysis framework. [Internet]. [cited 2018 Oct 1]. Available from: <https://root.cern.ch/>.
25. Ahn Y, Garruto RM. Estimations of body surface area in newborns. *Acta Paediatr* 2008;97:366–70.
26. Schmidt CWP. Body Surface Area (BSA). *Pediatric oncologic pharmacy: a complete guide to practice*. Cham: Springer International Publishing; 2019. p. 141.
27. Cohn SH, Dombrowski CS. Absolute measurement of whole-body potassium by gamma-ray spectrometry. *J Nucl Med* 1970;11:239–46.
28. Wang Z, St-Onge M-P, Lecumberri B, Pi-Sunyer FX, Heshka S, Wang J, Kotler DP, Gallagher D, Wielopolski L, Pierson RN, et al. Body cell mass: model development and validation at the cellular level of body composition. *Am J Physiol Endocrinol Metab* 2004;286: E123–8.
29. Kizirian N V, Markovic TP, Muirhead R, Brodie S, Garnett SP, Louie JCY, Petocz P, Ross GP, Brand-Miller JC. Macronutrient balance and dietary glycemic index in pregnancy predict neonatal body composition. *Nutrients* 2016;8:1–13.

30. McKenzie KM, Dissanayake HU, McMullan R, Caterson ID, Celermajer DS, Gordon A, Hyett J, Meroni A, Phang M, Raynes-Greenow C, et al. Quantity and quality of carbohydrate intake during pregnancy, newborn body fatness and cardiac autonomic control: conferred cardiovascular risk? *Nutrients* 2017;9:E1375.
31. Dissanayake HU, McMullan RL, Gordon A, Caterson ID, Celermajer DS, Phang M, Raynes-Greenow C, Skilton MR, Polson JW. Noninvasive assessment of autonomic function in human neonates born at the extremes of fetal growth spectrum. *Physiol Rep* 2018;6:e13682.
32. Castro NP, Euclides VV, Simões FA, Vaz-de-lima LRA, De Brito CA, Luzia LA, Devakumar D, Rondó PHC. The relationship between maternal plasma leptin and adiponectin concentrations and newborn adiposity. *Nutrients* 2017;9:E182.
33. Villar J, Puglia FA, Fenton TR, Cheikh Ismail L, Staines-Urias E, Giuliani F, Ohuma EO, Victora CG, Sullivan P, Barros FC, et al. Body composition at birth and its relationship with neonatal anthropometric ratios: the newborn body composition study of the INTERGROWTH-21st project. *Pediatr Res* 2017;82:305–16.
34. Andersen GS, Girma T, Wells JCK, Kæstel P, Michaelsen KF, Friis H. Fat and fat-free mass at birth: air displacement plethysmography measurements on 350 Ethiopian newborns. *Pediatr Res* 2011;70:501–6.
35. Andersen GS, Girma T, Wells JC, Kæstel P, Leventi M, Hother A-L, Michaelsen KF, Friis H. Body composition from birth to 6 mo of age in Ethiopian infants: reference data obtained by air-displacement plethysmography. *Am J Clin Nutr* 2013;98:885–94.
36. O'Connor C, O'Higgins A, Doolan A, Segurado R, Stuart B, Turner MJ, Kennelly MM. Birth weight and neonatal adiposity prediction using fractional limb volume obtained with 3D ultrasound. *Fetal Diagn Ther* 2014;36:44–8.
37. McCarthy FP, Khashan AS, Murray D, Kiely M, Hourihane JOB, Pasupathy D, Kenny LC. Parental physical and lifestyle factors and their association with newborn body composition. *BJOG* 2016;123:1824–9.
38. Breij LM, Steegers-Theunissen RPM, Briceno D, Hokken-Koelega ACS. Maternal and fetal determinants of neonatal body composition. *Horm Res Paediatr* 2015;84:388–95.
39. Pereira-da-Silva L, Cabo C, Moreira A, Virella D, Guerra T, Camoes T, Silva A, Neves R, Ferreira G. The adjusted effect of maternal body mass index, energy and macronutrient intakes during pregnancy, and gestational weight gain on body composition of full-term neonates. *Am J Perinatol* 2014;31:875–82.
40. Aris IM, Soh SE, Tint MT, Liang S, Chinnadurai A, Saw SM, Kwek K, Godfrey KM, Gluckman PD, Chong YS, et al. Body fat in Singaporean infants: development of body fat prediction equations in Asian newborns. *Eur J Clin Nutr* 2013;67:922–7.
41. Crume TL, Brinton JT, Shapiro A, Kaar J, Glueck DH, Siega-Riz AM, Dabelea D. Maternal dietary intake during pregnancy and offspring body composition: The Healthy Start Study. *Am J Obstet Gynecol* 2016;215:609.e1–8.
42. Josefson JL, Simons H, Zeiss DM, Metzger BE. Excessive gestational weight gain in the first trimester among women with normal glucose tolerance and resulting neonatal adiposity. *J Perinatol* 2016;36:1034–8.
43. Kadakia R, Zheng Y, Zhang Z, Zhang W, Hou L, Josefson JL. Maternal pre-pregnancy BMI downregulates neonatal cord blood LEP methylation. *Pediatr Obes* 2017;12:57–64.
44. Gallagher D, Rosenn B, Toro-Ramos T, Paley C, Gidwani S, Horowitz M, Crane J, Lin S, Thornton JC, Pi-Sunyer X. Greater neonatal fat-free mass and similar fat mass following a randomized trial to control excess gestational weight gain. *Obesity* 2018;26:578–87.
45. Intergrowth 21st. Standards and tools: newborn size: tables and graphs: weights. [Internet]. [cited 2019 Feb 16]. Available from: intergrowth21.tghn.org/newborn-size-birth/#ns1.
46. Villar J, Ismail LC, Victora CG, Ohuma EO, Bertino E, Altman DG, Lambert A, Papageorgiou AT, Carvalho M, Jaffer YA, et al. International standards for newborn weight, length, and head circumference by gestational age and sex: the Newborn Cross-Sectional Study of the INTERGROWTH-21st Project. *Lancet* 2014;384:857–68.
47. R Core Team. R: a language and environment for statistical computing. R Foundation for Statistical Computing, Vienna (Austria). [Internet]. [cited 2019 Mar 23]. Available from: <https://www.r-project.org/>.
48. Kv RK, Hemalatha R, Mamidi RS, Jj BG, Balakrishna N. Do South Indian newborn babies have higher fat percentage for a given birth weight? *Early Hum Dev* 2016;96:39–43.
49. Gianni ML, Roggero P, Taroni F, Liotto N, Piemontese P, Mosca F. Adiposity in small for gestational age preterm infants assessed at term equivalent age. *Arch Dis Child Fetal Neonatal Ed* 2009;94:F368–72.
50. Saenger P, Czernichow P, Hughes I, Reiter EO. Small for gestational age: short stature and beyond. *Endocr Rev* 2007;28:219–51.
51. Admassu B, Wells JCK, Girma T, Belachew T, Ritz C, Owino V, Abera M, Wibaek R, Michaelsen KF, Kæstel P, et al. Body composition during early infancy and its relation with body composition at 4 years of age in Jimma, an Ethiopian prospective cohort study. *Nutr Diabetes* 2018;8:46.
52. Admassu B, Wells JCK, Girma T, Andersen GS, Owino V, Belachew T, Michaelsen KF, Abera M, Wibaek R, Friis H, et al. Body composition at birth and height at 2 years: a prospective cohort study among children in Jimma, Ethiopia. *Pediatr Res* 2017;82:209–14.
53. Abera M, Tesfaye M, Girma T, Hanlon C, Andersen GS, Wells JC, Admassu B, Wibaek R, Friis H, Kæstel P. Relation between body composition at birth and child development at 2 years of age: a prospective cohort study among Ethiopian children. *Eur J Clin Nutr* 2017;71:1411–7.
54. Butte NF, Hopkinson JM, Wong WW, Smith EO, Ellis KJ. Body composition during the first 2 years of life: an updated reference. *Pediatr Res* 2000;47:578–85.
55. Fields DA, Krishnan S, Wisniewski AB. Sex differences in body composition early in life. *Gend Med* 2009;6:369–75.
56. Geary MPP, Pringle PJ, Rodeck CH, Kingdom JCP, Hindmarsh PC. Sexual dimorphism in the growth hormone and insulin-like growth factor axis at birth. *J Clin Endocrinol Metab* 2003;88:3708–14.
57. Ibáñez L, Sebastiani G, Lopez-Bermejo A, Díaz M, Gómez-Roig MD, de Zegher F. Gender specificity of body adiposity and circulating adiponectin, visfatin, insulin, and insulin growth factor-I at term birth: relation to prenatal growth. *J Clin Endocrinol Metab* 2008;93:2774–8.