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Body composition from birth to 6 months in term small for gestational age Indian infants: Effect of catch-up growth

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Short running title: Catch-up growth and body composition in SGA infants

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Abstract

The objective of this prospective observational study was to assess the growth and body composition of term small for gestational age (SGA) infants from birth to 6 months and evaluate the effect of catch-up growth (CUG) on body composition. Term SGA newborns were recruited at birth. Anthropometry and body composition were evaluated at 3 days, 6, 10 and 14 weeks, and 6 months. Fat and fat-free mass (FM and FFM) were compared between infants with and without CUG (increase in weight Z-score by >0.67) by air displacement plethysmography. Factors that could affect body composition and CUG, including parents' BMI and stature, infants' weight, gender and feeding were evaluated. 143 SGA newborns (66 boys) with birth weight of 2336 ± 214 g were enrolled; 109 were followed-up till 6 months. Median weight Z-score increased from -2.3 at birth to -1.3 at 6 months, with 51.9% of infants showing CUG. Infants with CUG had higher FM (1796 ± 491g vs. 1196 ± 474 g, $p<0.001$) but similar FFM (4969 ± 508g vs. 4870 ± 622g, $p=0.380$); and consequently higher FM% (26.5 ± 5.8 vs. 19.7 ± 6.9, $p<0.001$), compared to those without CUG. Lower birth weight, exclusive breastfeeding and higher parental stature were positively associated with CUG. In conclusion, CUG in term SGA infants in first 6 months of life was almost entirely attributable to greater gain in fat mass. Follow-up of this cohort will provide insight into the long-term effect of disproportionate gain in FM in early infancy in SGA babies.

Keywords: Low birth weight infants, accelerated growth, fat mass percentage, infancy growth, adiposity

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Introduction

South Asian phenotype is characterized by higher fat mass for the same BMI as compared to people of other ethnicities.[1] This is associated with a higher prevalence of cardiovascular disease and type 2 diabetes.[1] At the same time, the birth weight of Indian newborns is amongst the lowest in the world[2], with up to 47% of all newborns being small for gestational age (SGA).[3] suggesting a possible association between fetal growth restriction and higher later adiposity. While previous studies suggested that a 'thin-fat' phenotype, i.e., low weight but conserved fat mass is present right at birth in Indian newborns,[4] recent studies, including from our group,[5] using more robust techniques have shown that the fat mass percentage in Indian newborns is similar or rather lower compared to those reported for newborns in the US or Europe.[5,6] With this, the focus has now shifted to greater gain in fat mass during catch-up growth in infancy. In a previous small study, we had reported that low birth weight infants with catch-up growth (CUG) in the first 6 weeks had higher fat mass percentage at 9 months, compared to those without catch-up.[7] In another cohort of term healthy infants, we observed that CUG in weight between birth to 2 years was associated with higher fat mass index at 2 years.[8]

The hypothesis of accelerated fat gain during catch-up growth in infancy is interesting, as it represents a departure from fatalistic thinking (i.e., being born with a predetermined body composition) to a model of incremental or multiple-hit causality.[9] This opens up opportunities for intervention to modify the trajectory of fat versus lean mass gain. However, further research is needed to validate this hypothesis.

There is a paucity of direct measurements of fat and fat-free components of weight gain *during* the dynamic period of early infancy growth in term SGA newborns. The present study was undertaken with the aim of serially assessing the growth and body composition of term SGA infants from birth to 6 months; to evaluate the effect of CUG on body composition at 6 months of age, and assess the association of factors such as parents' weight and stature, infants' birth weight, gender and feeding) with weight gain velocity and body composition.

Participants and Methods:

This prospective birth cohort study was conducted at the All India Institute of Medical Sciences, New Delhi (AIIMS) and Safdarjung Hospital, New Delhi (SJH), with ethical approval from both these institutions. Full term SGA neonates (>37 weeks gestation with birth weight <10th centile for gestational age according to INTERGROWTH-21ststandards),[10] who were singleton, and whose parents were resident of New Delhi National Capital Region and willing for regular follow-up were enrolled at birth. The exclusion criteria were birth weight < 1600 g; gestational age not reliably known (1st trimester ultrasonography not done); major congenital malformations; maternal death or significant medical illness hampering her from feeding the baby; pre-existing or gestational diabetes; requirement of neonatal intensive care with intravenous fluids/ parenteral nutrition/ respiratory support/ phototherapy for > 3 days; and any obvious stigmata of intrauterine infections/ syndromic disorders. Enrolment was done after written informed voluntary consent from parents.

As we did not have data on weight catch-up growth (increase in weight Z-score >0.67) in Indian SGA infants when this work was initiated, we assumed the proportion of infants achieving CUG by 6 months as 50%. With precision of 10% and confidence level of 95%, the sample size was calculated as 97. The number to be enrolled was kept at 143 assuming up to 30% attrition (due to the traditional practice followed by many families of the mothers and babies going to live with the mothers' parents for several months, and the COVID-19 pandemic).

Eligible newborns were recruited within 24 -96 hours of birth. Gestational age was estimated based on the crown-rump length measurements in first trimester ultrasonography, which was performed either within the hospitals (AIIMS or SJH) or at private sonography centers. Maternal serial weights were noted from their antenatal clinic records. These had been measured using electronic weighing scales (to an accuracy of 100g). Maternal weight at her first antenatal visit in first trimester was used to calculate her BMI. Gestational weight gain (GWG) was calculated as the difference between the last weight measured prior to infant's birth and the first weight, and classified as inadequate, adequate or excessive in accordance with the Institute of Medicine 2009 guidelines.[11] Fathers' weights and both parents' heights were measured using an electronic weighing scale (accurate to 100g) and a wall-mounted

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stadiometer. Socioeconomic status (SES) was computed using the modified Kuppuswamy scale.[12]

All study related anthropometry and body composition measurements were done at AIIMS at the Pediatric Body Composition Lab. Newborns from SJH were recruited at discharge; the families made a detour through AIIMS (located across the street from SJH and connected via an underpass) on their way home after discharge. Infants' weight was measured to the accuracy of 1g using an electronic weighing balance (Seca 354, Hamburg, Germany), length to the accuracy of 0.1 cm using infant meter (Seca 417, Hamburg, Germany), and occipitofrontal head circumference (OFC) using non-stretch tape (Seca 212, Hamburg, Germany). Measurements were made in duplicate and averaged. Z-scores were calculated using WHO Anthro plus software (WHO 2010; version 3.1). BMI and Ponderal index[13] were calculated as (weight in Kg)/ (height in m)^2, and (weight in grams)*100/ (length in cm)^3, respectively. Infants were considered as *symmetrical* SGA if OFC and length were also below the 10th centile using the INTERGROWTH-21st charts, and *asymmetrical* if length, OFC, or both, were above the 10th centile.[14]

Body composition was measured by air displacement plethysmography (ADP) using Peapod infant body composition analyser (Cosmed, Concord, CA, USA). Fat and fat-free mass were derived assuming a fixed density of fat of 0.9007 g/ml,[15] and age and gender-specific fat-free mass density values.[16] The Peapod was calibrated daily with mass and volume phantoms. Body composition was summarized as fat mass percentage (FM%), fat mass index (FMI) and fat-free mass index (FFMI).

Follow-up visits: Follow up visits were scheduled at 6 (±1) weeks, 10 (±2) weeks and 14 (±3) weeks (to coincide with immunization visits) and at 6 (±1) months. At each visit, infants' weight, length and OFC were measured, and body composition was assessed. Feeding details of the infants were taken using the infant and young child feeding (IYCF) questionnaire.[17] If not exclusively breastfed, information on age till which exclusive breastfeeding was done, the type, amount and mode of supplementary feeding, and the reason for early initiation of supplementary feeds was noted. Catch-up growth during a period was defined as an increment of >0.67 in weight for age z-score (WAZ) during that period.[18]

Statistical analysis was done using STATA 12.0 College Station, Texas 77845 USA, Software. Descriptive data has been presented as mean ± SD, or as median (interquartile range (IQR)), if skewed. Fat and fat-free mass indices (FMI, FFMI) were calculated by dividing FM and FFM (in kg) by the square of length (in m) and reported as mean ± SD. For comparison between genders, independent t –test and Wilcoxon Ranksum test (for normally distributed and skewed data, respectively) were used. The proportion of infants who experienced CUG during the different time periods was calculated. The anthropometric and body composition measurements were compared between boys and girls, symmetrical and asymmetrical SGA, and infants with and without CUG using t-test. Effect of birth weight, gender, type of feeding, parents' BMI and stature, maternal education, parity and family's SES on CUG between birth to 6 months was evaluated by stepwise logistic regression; and effect of birth weight, type of feeding and weight Z-score change between birth to 6 months (ΔWAZ) on FFMI, FMI and FM% at 6 months was assessed by stepwise linear regression. P-value <0.05 was considered as significant.

Results

Description of the study cohort:

Total of 143 SGA newborns (66 boys) were enrolled. **Figure 1** presents the study flowchart. **Table 1** presents a summary of the parents' and infants' characteristics. The mean birth weight was 2336 ± 214 g, while the mean maternal BMI in the first trimester was 20.9 ± 3.4 Kg/m^2. Sixteen babies (11.2%) were symmetrical SGA with length and OFC also below the 10^{th} centile. Their birth weight (2205 ± 239g vs. 2352 ± 206g, *p*=0.009) and maternal BMI (18.8±3.2 Kg/m2 vs. 21.2±3.4 Kg/m2, *p*=0.007) were lower in comparison to the asymmetrical SGA babies.

The birth and socio-demographic characteristics of the 104 infants for whom body composition data was available at 6 months, vs. the 39 infants for whom this data was not available were similar (birth weight 2334 ± 216 vs. 2341 ± 213 g, *p*=0.856; male/ female 47(45%)/57(55%) vs. 19(49%)/20(51%), *p*= 0.706; SES (upper or upper middle/ lower middle/ upper lower/ lower) 10(9.5%)/ 23(22%)/ 67(64.5%)/ 4(4%) vs. 6(16%)/ 12(31%)/20 (50.5%)/1(2.5%) *p*= 0.612, respectively).

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Body composition (FM%, FMI, FFMI) at birth and influence of various factors:

The anthropometric and body composition data at birth is presented in **Table 2**. The mean FM% was 5.5 ± 2.8. Gender comparison showed that the fat-free mass was significantly higher in boys (2145 ± 210g vs. 2061 ± 201g, p = 0.014). FM% was 5.8 ± 3.1% in girls, compared to 5.0 ± 2.5% in boys, but the difference was not statistically significant. FMI and FFMI were similar in boys and girls.

Birth weight showed a direct correlation with FFMI (beta = 0.515, p<0.001), FMI (beta 0.161, p = 0.055), as well as FM% (beta 0.138, p = 0.099); however, this was statistically significant only for FFMI. Asymmetrical SGA newborns had lower FM% than the symmetrical SGA newborns (5.3 ± 2.5% vs. 7.0 ± 4.5%, p = 0.024). Maternal BMI and gestational weight gain (GWG) did not have a significant effect on FM%, FMI or FFMI at birth.

Longitudinal evaluation from birth to 6 months:

The serial anthropometric and body composition data of all the infants who presented for follow-up at birth, 6 weeks, 10 weeks, 14 weeks and 6 months is presented in **Table 2**. The median Z-scores of weight, length and BMI improved gradually, with the most marked improvement between 6 and 14 weeks. FM% and FMI showed a three-fold rise between birth to 6 weeks, with a further gradual increase up to 14 weeks, followed by plateauing. The rise in FFMI was gradual, with no plateauing till 6 months.

Gender comparison at 6 months showed that boys had significantly higher weight, length, and FFMI (12.1± 0.8 Kg/m^2 vs. 11.3 ± 1.0 Kg/m^2, p<0.001); while the gender difference in FM% and FMI (both higher in girls) was not statistically significant.

Catch-up growth in weight during different time periods, and the effect on body composition

CUG was noted in 19 out of 89 (21.4%) of the infants between births to 6 weeks. Between birth to 10 weeks, birth to 14 weeks and birth to 6 months, the proportion of infants who had CUG was 34.4%, 44.4% and 51.9%, respectively. The comparison of anthropometry and body composition in infants with and without catch-up growth between birth to 6 weeks, 10 weeks, 14 weeks, and 6 months is presented in **Table 3**. At 6 and 10 weeks, those with CUG had higher FMI as well as FFMI. However in terms of percentage of body weight, fat mass gain was disproportionately higher. At 14 weeks and 6 months, the difference in body composition became even more marked. The difference in weight between CUG and non-CUG groups at 14 weeks and 6 months was almost entirely due to the higher gain in fat mass (**Table 3**). **Figures 2a and 2b** summarize the serial weight, length and BMI Z-scores, and the FMI and FFMI, respectively, of infants with and without CUG by 6 months of age.

The change in WAZ between birth to 6 months (ΔWAZ) was positively associated with FM% (beta = 0.593, $p<0.001$) (**Figure 3)**, and FMI (beta = 0.657, $p<0.001$) at 6 months, but not FFMI (beta = 0.038, $R^2 = 0.002$, $p = 0.699$).

Effect of exclusive breastfeeding on catch-up growth

Sixty eight of the 104 infants assessed at 6 months (65.4%) had been exclusively breastfed for at least five months, while 36 had been initiated on supplemental feeds before 5 months. The predominant reason for early introduction of supplemental feeds was the perceived poor weight gain of the infant. CUG was present in 40/68 (58.8%) of the exclusively breastfed group, compared to 14/36 (38.9%) of the mixed fed group, $p=0.006$. The weight and FFMI at 6 months were similar in the two groups but FM% (24.8 ± 7.2% vs. 20.2 ± 6.3%, $p=0.002$) was higher in the exclusively breastfed compared to mixed fed group.

Other factors influencing CUG: Table 4 summarizes the effect of various parameters such as the infants' birth weight, symmetrical vs. asymmetrical SGA status, gender, parents' weight and height and socioeconomic status on CUG as a binary variable. The effect of birth weight, feeding and ΔWAZ on FMI and FFMI is also summarized in **Table 4**.

Supplementary table 1 provides a comparison of maternal parameters, and infants' anthropometry and body composition of symmetrical and asymmetrical SGA infants at birth and 6 months of age.

Discussion

While there are previous studies that suggest that catch-up growth in infancy or in the first few years of life may be associated with higher adiposity in childhood[8,19,20],or adulthood,[21, 22] there is paucity of literature on the composition of the catch-up weight gain *during* the most dynamic periods of the first few weeks to months of life in SGA infants. The key observations in the present study are that in healthy, predominantly breastfed term SGA Indian infants, there is an increase in median weight and length Z-scores from -2.3 to -1.3, and from -1.4 to -0.9, respectively, between birth and six months. Mean FM% increases from 5.5% at birth to 23.4% at 14 weeks, with plateauing between 14 weeks to 6 months. Infants who had catch-up growth in weight had significantly higher FM% compared to those without catch-up. The mean difference in FM between the infants with and without CUG was 600 g at 6 months, which comprised 82% of the observed difference in weight.

The mean FM% at birth of the SGA infants in our study is very similar to that reported for term SGA newborns from the Oxford site of the INTERGROWTH-21st study (5.7 ± 3.0%),[23] and much lower than that of term AGA newborns measured using Peapod in a previous study from our centre (7.9 ± 2.9%) (Tak AS, Jain V, et al, unpublished data), thus providing further evidence against the previous hypothesis that fetal growth restriction is associated with conserved fat mass in Indian newborns.[4] At 14 weeks, the mean fat and fat-free mass of the present cohort were 1.3 ± 0.5 Kg, and 4.0 ± 0.5 kg, respectively; while that of term AGA infants (n=120) in a previous study from our group (body composition assessment by isotope dilution)[8] were 1.3 ± 0.5 Kg and 4.5 ± 0.6 Kg, respectively. Thus there was complete catch-up in fat mass in the SGA infants by the age of 14 weeks, but persistent deficit in FFM. There is only one previous study that has reported body composition of SGA infants longitudinally during infancy. In this Swedish study (n=25), FM% increased from 3.7% at birth to 25.8% at 16.5 weeks.[24] Comparison with other longitudinal studies in infancy (in term healthy infants, not SGA) as shown in **Supplementary Figure 1,** also indicates that our SGA cohort had a complete catch-up in FM% by the age of 3-4 months.[25-28]

The chief determinant of weight CUG between birth to 6 months were lower birth weights of the infants and higher stature of the parents. Taken together, these reflect a mismatch between the infants' size at birth and their genetic potential. As catch-up is a physiological phenomenon, by which the organism tries to realign its growth to the genetically determined trajectory after deviating from it due to an insult,[29, 30] the babies with a greater mismatch may have better feeding behavior (demand more, suckle better), and better weight gain.[31] Hence, these babies would be more likely to be continued on exclusive breastfeeding. On the other hand babies with a lower degree of mismatch, may have lower feed intake and lower weight gain, prompting their mothers to add formula (as was reported by mothers in our cohort). Therefore, we speculate that higher rates of exclusive breastfeeding among those with CUG in our cohort may be more of a reflection of babies' growth pattern, rather than the cause.

The major strengths of this study are its prospective design with analysis of various factors affecting catch-up growth and body composition in infancy, use of standardized definitions for SGA and catch-up growth, and body composition assessment by Peapod. The limitations are an attrition of the cohort, not having all data at all the time points (owing to the pandemic situation), and the first trimester ultrasonography and maternal weight measurements having been done as part of clinical care, and therefore not following standardized methodology. Another limitation is that the results of this study are not applicable to term SGA infants with birth weight <1600 g, and to preterm SGA infants.

To conclude, the present study showed that the main drivers of catch-up weight gain in the first 6 months are lower birth weight, exclusive breastfeeding for ≥ 5 months, and taller stature of parents; and the chief component of the catch-up weight gain is fat mass, accounting for more than eighty percent of the extra weight in the group with catch-up weight gain. Comparison with term AGA infants from a previous cohort from our centre suggested that SGA infants have a complete catch-up in fat mass by 3-4 months, but persistent deficit in fat-free mass. Further follow-up of this cohort will help in understanding whether these early differences in body composition associated with catch-up growth persist into later childhood, and whether these have any effect on cardio-metabolic parameters.

Ethical Approval:

IECPG-525/29.08.2019, RT-04/26.09.2019 and IEC/VMMC/SJH/Project/ 2019-12/ 93

Disclosure statement

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Conflict of Interest: None of the authors have any conflicts of interest.

Authorship

BK recruited the newborns, conducted the measurements, analyzed the data, and drafted the initial manuscript. PA, HC and RA facilitated the enrolment of newborns, supervised data collection and provided constructive inputs for the manuscript. VJ conceptualized and designed the study, interpreted the data, co-drafted the manuscript, critically reviewed and revised it, and will act as guarantor. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Abbreviations:

SGA: Small for gestational age

CUG: Catch-up growth

WAZ: weight for age Z-score

BMI: Body mass index

ΔWAZ: Change in WAZ between birth to 6 months

GWG: Gestational weight gain

FM: Fat mass

FFM: Fat-free mass

FM%: Fat mass percentage

FMI: Fat mass index

FFMI: Fat-free mass index

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Table 1. Baseline description of the study cohort

Parents' characteristics (N=143)	**Mean ± SD or N (%)**
Mothers' age, y	25.4 ± 4.4
Primipara, N (%)	107 (75)
Mother's weight in first trimester (kg)	49.0 ± 9.0
Mother's height, cm	152.8 ± 5.4
Mothers' BMI in first trimester, kg/m2 Maternal BMI categories, N (%): <18.5Kg/m2 18.5-24.9Kg/m2 >/=25Kg/m2	20.9 ± 3.4 31 (21.7) 98 (68.5) 14 (9.8)
Gestational weight gain (GWG), kg GWG categories*, N (%): Inadequate Adequate Excessive	8.3 ± 3.5 120 (83.9) 19 (13.3) 4 (2.8)
Fathers' height, cm	166 ± 7.1
Fathers' BMI, kg/m2	23.6 ± 3.4
Socioeconomic status Upper/ Upper middle Lower middle Upper lower Lower	 16 (11) 34 (24) 88 (61) 5 (4)
Infants' characteristics (N=143)	**Mean ± SD or Median (IQR) or N (%)**
Boys/ Girls, N (%)	66 (46.2) / 77 (53.8)
Gestational age, weeks	38.6 ± 1.3

Birth weight (g) Categories, N %) < 2000g 2000-2500g >2500g	2336 ± 214 6(4.2) 101(70.6) 36(25.2)
Birth length, cm <10th centile, N (%)	46.9 ± 1.4 58 (40.6%)
Ponderal index (g/cm3)	2.27 ± 0.19
Head circumference, cm (median (IQR)) <10th centile, N (%)	32.9 (30.4–35.5) 25 (17.5)
Symmetrical SGA/ Asymmetrical SGA, N (%)	16 (11.2) /127(88.8)

*****According to Institute of Medicine 2009 guidelines [11]

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Table 2. Serial evaluation of anthropometry and body composition from birth to 6 months

Variable	Birth	6 weeks	10 weeks	14 weeks	6 months
N	143	89	61	72	104
M/ F	66/77	44/45	25/36	30/42	47/57
Age at visit	3.1 ± 1.5 days	6.7 ± 0.9 weeks	11 ± 1.3 weeks	16.4 ± 2.1 weeks	6.3 ± 1.0 months
Weight, g	2336 ± 214	3661 ± 562	4495 ± 668	5316 ± 692	6460 ± 799
WAZ#	-2.3 (-2.5,-1.9)	-2.2 (-2.9,-1.5)	-2.0 (-2.8,-1.2)	-1.6 (-2.4,-1)	-1.3(-2.4,-0.8)
Length, cm	46.9 ± 1.4	53.4 ± 2.2	56.5 ± 2.7	60.1 ± 2.4	65.0 ± 2.2
LAZ#	-1.4 (-1.7,-1.0)	-1.4 (-2.1,-0.8)	-1.1(-2, -0.8)	-1.0 (-1.8,-0.2)	-0.9 (-1.4,-0.3)
BMI, kg/m^2	10.1 ± 0.8	12.8 ± 1.4	14.0 ± 1.7	14.7 ± 1.3	15.3 ± 1.5
BMIZ#	-2.5 (-3.0,-1.9)	-2.1 (-2.7,-1.4)	-1.8 (-2.5,-1)	-1.6 (-2.4,-0.8)	-1.4 (-2.1,-0.6)
Fat mass, g	129 ± 89	621 ± 252	919 ± 384	1264 ± 462	1508 ± 567
Fat free mass, g	2100 ± 211	3077 ± 409	3610 ± 526	4034 ± 457	4922 ± 562
FM,%	5.5 ± 2.8	16.5 ± 5.5	19.9 ± 6.8	23.4 ± 7.0	23.2 ± 7.2
FMI, kg/m^2	0.6 ± 0.4	2.2 ± 0.8	2.9 ± 1.2	3.5 ± 1.2	3.6 ± 1.3
FFMI, kg/m^2	9.5 ± 0.8	10.8 ± 1.1	11.3 ± 1.3	11.1 ± 0.9	11.6 ± 1.0

N: number, WAZ: weight for age Z-score, LAZ: length for age Z-score, BMIZ: BMI for age Z-score, FM: fat mass, FMI: fat mass index; FFMI: fat-free mass index

Data presented as median (IQR)

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Table 3. Comparison of anthropometry and body composition between infants who had weight catch-up growth versus those who did not, between birth to 6 weeks, 10 weeks, 14 weeks and 6 months

Variables	**With catch-up growth**	**Without catch-up growth**	**P-value**	**With catch-up growth**	**Without catch-up growth**	**P-value**
	At 6 weeks			**At 10 weeks**		
	N=19	**N=70**		**N=21**	**N=40**	
Weight, g	4096 ± 286	3544 ± 562	<0.001	4960 ± 418	4251 ± 648	<0.001
WAZ#	-1.4 (-1.6,-1.0)	-2.4 (-3.2,-1.9)	<0.001	-1.0(-1.2,-0.7)	-2.4(-3.0,-2.0)	<0.001
Length, cm	54.0 ± 0.7	53.2 ± 2.3	0.172	57.3 ± 2.9	56.2 ± 2.6	0.139
LAZ#	-1.1 (-1.4,-0.8)	-1.5 (-2.4,-0.8)	0.070	-0.8 (-1.0,-0.3)	-1.7(-2.1,-1.0)	0.024
BMI, kg/m^2	14.0 ± 1.3	12.5 ± 1.4	<0.001	15.2 ± 1.7	13.4 ± 1.3	<0.001
FM, g	792 ± 141	578 ± 256	0.001	1145 ± 327	800 ± 362	<0.001
FFM, g	3290 ± 260	3022 ± 423	0.012	3914 ± 608	3450 ± 399	<0.001
FM,%	19.2 ± 5.7	15.8 ± 5.7	0.015	23.3 ± 6.1	18.2 ± 6.5	0.004
FMI, kg/m^2	2.7 ± 0.5	2.0 ± 0.9	0.001	3.5 ± 1.1	2.5 ± 1.0	<0.001
FFMI, kg/m^2	11.3 ± 1.2	10.7 ± 1.2	0.022	12.0 ± 1.8	10.9 ± 0.9	0.003
	At 14 weeks			**At 6 months**		
	N=32	**N=40**		**N=54**	**N=50**	
Weight, g	5754 ± 544	4966 ± 596	<0.001	6796 ± 666	6057 ± 751	<0.001
WAZ#	-0.9 (-1.4,-0.7)	-2.2 (-2.8,-1.7)	<0.001	-0.9 (-1.3,-0.5)	-2.4 (-2.9,-1.6)	<0.001
Length, cm	60.9 ± 1.9	59.5 ± 2.6	0.010	65.3 ± 2.1	64.6 ± 2.3	0.113
LAZ#	-0.8 (-1.0,-	-1.2 (-2.1,-	0.005	-0.7 (-	-1.2 (-2.0,-	<0.001

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	0.3)	0.5)		1.1,0.1)	0.7)	
BMI, kg/m^2	15.5 ± 1.1	14.0 ± 1.1	<0.001	15.9 ± 1.2	14.5 ± 1.2	<0.001
FM, g	1552 ± 373	1034 ± 395	<0.001	1796 ± 491	1196 ± 474	<0.001
FFM, g	4174 ± 405	3922 ± 470	0.018	4969 ± 508	4870 ± 622	0.380
FM,%	27.0 ± 5.2	20.5 ± 6.9	<0.001	26.5 ± 5.8	19.7 ± 6.9	<0.001
FMI, kg/m^2	4.2 ± 1.0	2.9 ± 1.0	<0.001	4.2 ± 1.1	2.9 ± 1.1	<0.001
FFMI, kg/m^2	11.2 ± 0.8	11.1 ± 1.0	0.479	11.6 ± 0.9	11.6 ± 1.1	0.980

WAZ: weight for age Z-score, LAZ: length for age Z-score, FM: fat mass; FFM: fat- free mass; FMI: fat mass index; FFMI: fat-free mass index

#Data presented as median (IQR)

Table 4. Regression analysis of catch-up growth and body composition at 6 months with predictor variables

Catch-up growth (Δ WAZ >0.67) between birth to 6 months						
Variable	Unadjusted			Adjusted		
	Odds ratio	95% C.I.	*p* value	Odds ratio	95% C.I.	*p* value
Birth weight (kg)	0.14	0.02 – 0.94	**0.043**	0.04	0.003 – 0.55	**0.021**
Female vs. male	1.99	0.91 – 4.35	0.083	1.17	0.43 – 3.14	0.762
Exclusively breastfed for ≥ 5 mo vs. <5 mo	2.24	0.98 - 5.12	**0.005**	2.23	0.87 – 5.74	0.096
Asymmetrical vs. Symmetrical SGA	1.52	0.49 – 4.75	0.401	1.89	0.41 – 8.74	0.410
Mothers' weight (kg)	1.04	0.99 - 1.09	0.051	1.02	1.00 – 1.22	0.501
Mothers' height (cm)	1.12	1.03 - 1.21	**0.004**	1.10	1.00 – 1.23	**0.046**
Multiparous vs. primiparous mothers	1.29	0.56 - 2.97	0.552	1.40	0.53 – 3.73	0.492
Fathers' weight (kg)	1.03	0.99 - 1.08	0.130	1.00	0.95 – 1.07	0.853
Fathers' height (cm)	1.07	1.01 - 1.13	**0.026**	1.04	0.96 – 1.12	0.312
Socioeconomic status	1.02	0.61 – 1.69	0.903	1.30	0.62 – 2.60	0.501
Fat mass index at 6 months (kg/m2)						
Variable	Unadjusted			Adjusted		
	Beta	95% C.I.	*p* value	Beta	95% C.I.	R^2, *p* value
Birth weight (kg)	0.69	-0.77 – 1.61	0.486	0.216	0.451 – 2.178	0.494, <0.001
ΔWAZ (birth to 6 mo)	0.657	0.72 – 1.36	**<0.001**	0.670	0.742 – 1.149	
Exclusively breastfed for ≥ 5 mo vs. <5 mo	0.292	0.29 – 1.32	**0.003**	0.178	0.102 – 0.879	
Fat-free mass index at 6 months (kg/m2)						
Variable	Unadjusted			Adjusted		
	Beta	95% C.I.	*p* value	Beta	95% C.I.	R^2, *p* value
Birth weight (kg)	0.429	1.18 – 2.83	**<0.001**	0.456	1.31 – 2.97	0.216, <0.001
ΔWAZ (birth to 6 mo)	0.038	- 0.17 – 2.84	0.697	0.169	-0.011 – 0.380	
Exclusively breastfed for ≥ 5 mo vs. <5 mo	-0.186	-0.80 – 0.014	0.059	-0.198	-0.793 - -0.047	

SGA: small for gestational age, ΔWAZ: Change in weight for age weight for age Z-score between birth to 6 months

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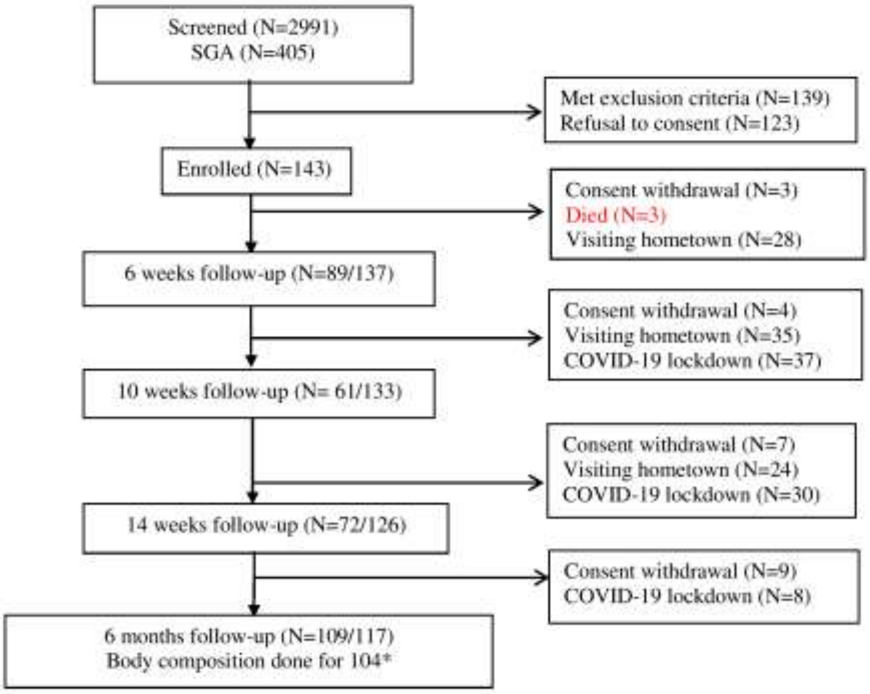
Figure1. Study flow: Enrolment and follow-up numbers of the study cohort



* Body composition by Peapod could not be assessed in 5infants at the six month visit, either due to their larger size relative to the chamber, or excessive crying. Of these, three infants had catch-up growth.
At each visit, the denominator reflects the number of babies remaining in the study.

Figure 1.Study flow: Enrolment and follow-up numbers of the study cohort

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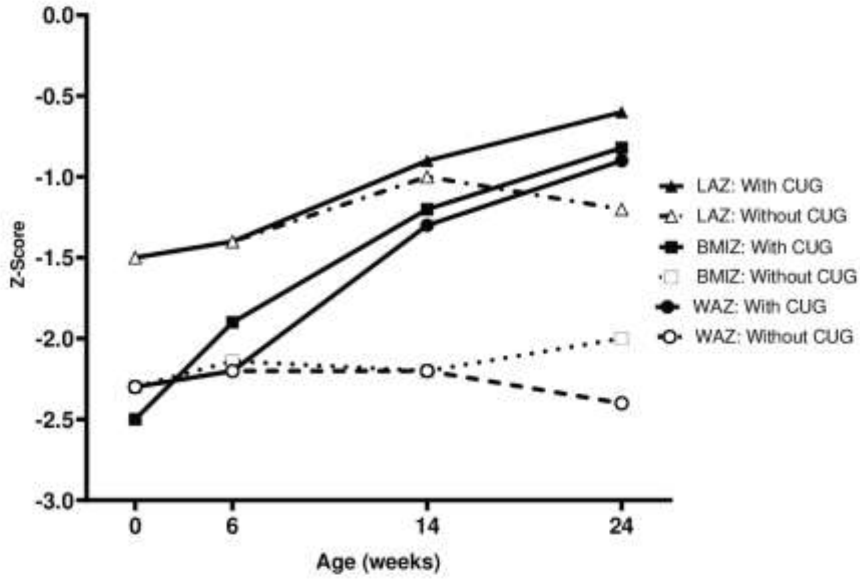

Figure 2a

Figure 2a. Longitudinal Z-scores for weight, length and BMI from birth to 6 months among infants with and without CUG (in a subset of 53 infants with data at all time points)

WAZ: weight for age z-score, LAZ: length for age z-score, BMIZ: BMI for age z-score, CUG: catch-up growth

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Figure 2b

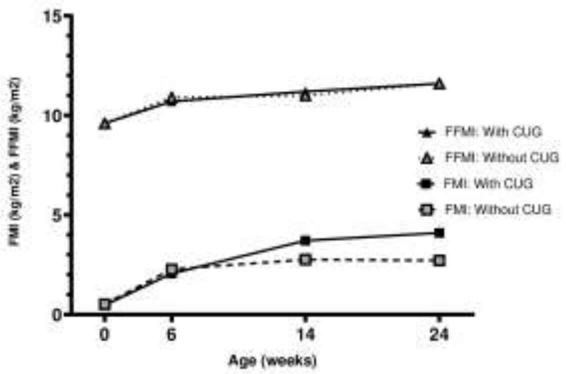

Figure 2b. Longitudinal mean fat-free mass index (FFMI) and fat mass index (FMI) from birth to 6 months among infants with and without CUG (in a subset of 53 infants with data at all time points)

FMI: fat mass index, FFMI: fat free mass index, CUG: catch-up growth

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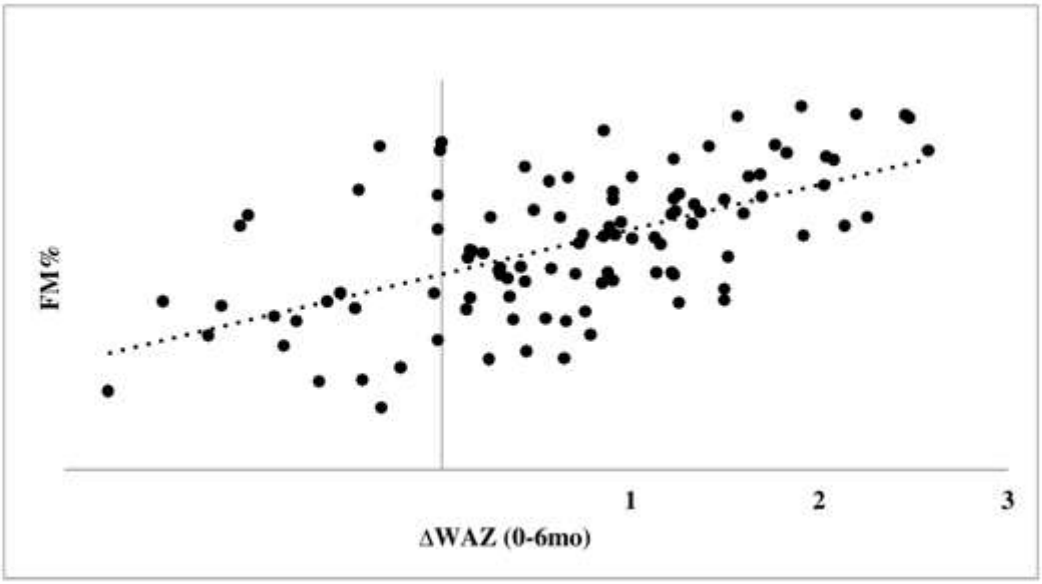

Figure 3. Scatter plot of change in weight for age z-score between birth to 6 months (ΔWAZ) with fat mass percentage (FM%) at 6 months (N=104)

FM%: fat mass percentage; CUG: catch-up growth

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