

Body composition at birth and height at 2 years: A prospective cohort study among children in Jimma, Ethiopia

Bitiya Admassu^{1*}, Jonatan C. Wells², Tsinuel Girma³, Gregers S. Andersen⁴, Victor Owino⁵, Tefera Belachew¹, Kim F. Michaelsen⁶, Mubarek Abera⁷, Rasmus Wibaek^{4,6}, Henrik Friis⁶, Pernille Kæstel⁶

Short title: Body composition at birth and height

Affiliation

¹ Department of Population and Family Health, College of Public Health and Medical Sciences, Jimma University, Jimma, Ethiopia ; ² Childhood Nutrition Research Centre, UCL Institute of Child Health London WC1N 1EH, UK; ³ Department of Pediatrics and Child Health, College of Public Health and Medical Sciences, Jimma University, Jimma, Ethiopia ; ⁴ Steno Diabetes Center, Copenhagen, Gentofte, Denmark; ⁵ International Atomic Energy Agency, Vienna, Austria; ⁶ Department of Nutrition, Exercise and Sports, University of Copenhagen, Copenhagen, Denmark; ⁷ Department of Psychiatry, College of Public Health and Medical Sciences, Jimma University, Jimma, Ethiopia

Email:

BA: bitiyaa@yahoo.com; JCW: jonathan.wells@ucl.ac.uk; TG: tsinuel@yahoo.com; GA: gregers.stig.andersen@regionh.dk; VO: vowino@hotmail.com; TB: teferabelachew@gmail.com; KFM: kfm@nexs.ku.dk; MA: abmubarek@gmail.com; RW: rwibaek@gmail.com; HF: hfr@nexs.ku.dk; PK: pernille.kaestel@gmail.com

*Corresponding author: Bitiya Admassu, Department of Population and Family Health, College of Public Health and Medical Sciences, Jimma University, Ethiopia, PO Box 378, Jimma, Ethiopia. bitiyaa@yahoo.com +251 911999382

Funding Source: Danish Council for Strategic Research—Programme Commission on Food and Health; Danida through the Consultative Research Committee for Development Research (104.Dan.8-1207)

Financial Disclosure: None.

Conflict of Interest: None of the authors reported a conflict of interest related to the study.

Category of study: Population study (Prospective cohort study)

Author's contribution

The authors' responsibilities were as follows—BA, HF, JW, TG, GSA and PK: designed the study; BA, GSA, PK, MA, RW, JCW, TG and HF have supervised the data collection; BA: analyzed the data, drafted the manuscript and had primary responsibility for the final content of the manuscript. All Authors: contributed to the manuscript revisions and read the final manuscript and approved for submission.

Abstract

Background: Low birth weight is associated with childhood stunting, but equivalent associations for birth body composition (BC) remain unknown.

Objective: To assess associations of BC with height-for-age Z score (HAZ) at 2 years of age.

Methods: In a prospective cohort study, fat mass (FM) and fat-free mass (FFM) were measured using air-displacement plethysmography within 48 hours of birth. Linear regression models were applied to study the relationship between BC at birth and HAZ at 24 months (± 3 months).

Results: A total of 268 children with height assessment at 2 years were included. Mean \pm SD HAZ at 2 years of age was -1.2 ± 1.2 , with 25.8% classified as stunted (HAZ < -2 SD). FFM at birth was positively associated with HAZ at 2 years, independent of length at birth. When adjusted for potential confounders, HAZ at 2 years was 0.73 higher for each additional kg FFM at birth ($\beta=0.73$, 95%CI (0.08, 1.38)). FM was not associated with HAZ at 2 years in any model.

Conclusion: The FFM component of birth weight, independent of length, explains variability in HAZ at 2 years. Further studies are required to explore how changes in early infant BC are associated with linear growth.

Introduction

Despite significant advances in child nutrition and health, under-nutrition remains one of the main public health challenges in low- and middle-income countries (1). Globally, around 159 million children less than 5 years are stunted (height-for-age Z score (HAZ) ≤ -2) (2). In Ethiopia, stunting affected 24% and 42% of children less than five years in urban and rural areas, respectively (3).

Stunting is a well-known risk factor for childhood mortality and impaired development (4,5). It results in poor learning capacity and school performance in childhood, and reduced earning and work capacity in adulthood (4–6). This chronic nutritional problem occurs during the crucial period of pregnancy and the first 2 years of life, the ‘first 1000 days’, during which growth and nutrition have lifelong health implications (4,7).

Stunting in childhood is the result of numerous circumstances and determinants, including antenatal and postnatal malnutrition (8) and is not uniformly understood (4,8). Small size at birth, low maternal height, inappropriate feeding and a high number of infections, especially diarrhea, have been associated with stunting (9,10). Although numerous authors identified low birth weight as one of the risk factors for childhood stunting, body composition has received less attention. BC in children is now understood to be an indicator of current health status (11) and is associated with disease in later life (12,13). In this regard, studies that investigate BC in childhood are important towards a better understanding of stunting in children.

Presently, however, only few studies have investigated the relation between BC at birth and linear growth faltering (10,14–16). In those studies body composition was assessed using simple

anthropometric indices such as body weight, body mass index and skin fold measurements; which may not be accurate and precise measurements of BC in children and may not adequately reflect total body fatness during infancy (17). To the best of our knowledge, no previous study has investigated BC as a predictor of HAZ.

It was recently shown in the Ethiopian Infant Anthropometry and Body Composition cohort (iABC) that neonates with the same birth weight had a large variation in FM and FFM (18). In addition, the study demonstrated that groups with lower birth weight such as girls and first born children had reduced FFM but not significantly less FM. This indicates that studies using crude measurement techniques like body weight and body mass index might miss the potential effects of variation in BC on health outcomes.

In this analysis, we present findings from the 2-years follow-up of the iABC study. The aim of the study was to investigate the association between birth body composition and HAZ at 2 years of age.

Subjects and Methods

Study design, setting and participants

This prospective cohort study was conducted at Jimma University Specialized Hospital (JUSH) in Jimma Town, Ethiopia, from January 2009 to August 2014.

Data for the present study was collected as part of the iABC cohort study which has been described in detail elsewhere (18,19). Briefly, eligible mother- infant pairs were recruited among women gave birth at the maternity ward at JUSH. Women and their newborn were eligible if they were living in Jimma Town and the child was born at term (gestational age of ≥ 37 weeks,

using Ballard score assessment) with a birth weight ≥ 1500 g and without congenital malformation. Women and newborns were examined within 48-hours after birth. Newborns with serious medical conditions observed during baseline examination were not included. A total of 617 infants were recruited at birth. Of these, 268 children had height measurements at 2 year and were analyzed in this study.

Data collection

Anthropometric measurements

Length was measured in supine position for children below 2 years whereas height was measured in standing for those 2 years and above according to WHO guidelines. Anthropometric measurements were made at 2year ± 3 month. Length/height was measured in duplicate to the nearest 0.1 cm using a SECA 416 length board (SECA, Hamburg, Germany) and a SECA 213 portable stadiometer according to WHO recommendations (20) and the average was used for length/height analysis. For this paper, height was operationalized as height-for-age Z-scores based on the WHO growth standards (21), and stunting was defined as height-for-age Z-score below minus two standard deviations (-2 SD).

Birth weight, FM and FFM were measured within 48 hours after birth to the nearest 1 g using a Peapod®, an infant air-displacement plethysmograph (ADP) specifically developed for measurement of infant BC (COSMED, Rome, Italy) (22). ADP is considered a fast, safe, precise, and accurate densitometry technique to assess BC in neonates and infants (23). The theory and standard operating procedures used in the present study has been described elsewhere (19). ADP is a two component model which divides body weight into FFM and FM. FM consists of only fat and free from water while FFM includes: protein, water and mineral (osseous and non osseous).

Questionnaire data at birth

Data were collected by trained research nurses using a structured and pretested questionnaire.

Information on maternal age and parental education was obtained. Data on socio-economic status such as water quality, consumer durables (electricity, telephone, mobile, television, radio, refrigerator, stove, car, motor cycle and electric injera mitad) and toilet facility were collected at the time of delivery.

Questionnaire data at 2 years of age

Hospitalization was assessed using the question “Was the child ever admitted to any health facilities for treatment since birth” and the response was recorded as yes/no.

Mothers were asked about the milk intake of their child within one week before the interview at two years of age. Milk intake of the child was described by total frequency of milk intake other than breast milk during the past one week. Then, the response was categorized as not consumed, regularly consumed (1-6 days/wk) or consumed every day (7 days).

Data handling and statistical analysis

Data were double entered using EpiData (version 3) (Odense, Denmark, 2003-2008). STATA/IC 12.1 (StataCorp, College Station, TX) was used for data analysis. The Zscore06 Stata command was used for the calculation of anthropometric z-scores using the 2006 WHO child growth standards (24).

Mean \pm standard deviation (SD) was calculated for symmetric continuous variables. A wealth index was constructed from three overall socioeconomic categories: drinking water quality (four items, response 0 or 1), consumer durables (ten items, response 0 or 1) and toilet facility (five

items, response 0 or 1). The wealth index score was generated from the data using Principal Components Analysis (PCA); the first PCA factor that explained most of the variation was used to group study households into wealth quintiles (25). Chi-2 tests and *t*- tests were used to examine the differences between those included and lost to follow up. Simple and multiple linear regression analysis were performed. Linear regression analysis was applied to examine the association between body compositions at birth as the main exposure variables and HAZ at 2 years of age as the outcome. The contribution of other covariates to HAZ at 2 years of age was evaluated by adding those variables to the linear regression models where we have the main exposure variable.

Separate multiple linear regression models for FFM and FM were developed (adjusting for early infant characteristics, cow milk intake, morbidity factor and parental factors. **Model 1:** FFM or FM were included in the model as a continuous variable and birth length, sex and current age were adjusted for. **Model 2:** Same as model 1 plus cow milk intake, breast feeding and hospitalization **Model 3:** Same as model 2 plus maternal age, maternal education and paternal education. **Model 4 (Fully adjusted model):** Same as model 3 plus parental wealth index.

Variables were considered for the multiple regression models if they were main exposure variable; potential confounding factors identified a priori from the literature or affected the estimate of main exposure (birth FM and FFM). A p-value < 0.05 was considered significant.

Scatter plots of the residuals versus the independent variables and the predicted values were examined to determine if there were patterns diverging from a normality distribution. Variance Inflation Factor (VIF) and the Tolerance tests were used to test for the presence of multi collinearity among the independent variables. VIF less than 10 was accepted. The results were

presented using β -coefficients and 95% confidence intervals. Also, presence of interaction was checked between sex, wealth index, FM and FFM and a p-value < 0.05 considered as significant level.

Ethical considerations

Ethical approval was obtained from Jimma University, College of Public Health and Medical Science's Institutional Review Board (reference RPO/56/2001). Written informed consent was obtained from each mother or guardian before commencing data collection. Participants who were unable to sign gave thumb print. To maintain confidentiality, any identifiers were removed from the data before analysis. There were no risks associated with any of the examinations. Children found to be ill at any examinations were referred for diagnosis and treatment to Jimma University Specialized Hospital.

Results

Of 617 children recruited at birth, 271 (44.0%) were followed up for two years. Of those, 268 (98.9%) who had height measurements at 2 years of age were included in the study. A flow chart of the follow-up of study participants is presented in figure 1.

The mean \pm SD gestational age was 38.9 ± 1.0 week. The mean \pm SD FM at birth was 0.2 ± 0.2 kg while FFM was 2.8 ± 0.3 kg (**Table 1**). At follow-up, mean \pm SD age of children was 24.3 ± 0.8 months. The mean HAZ at 2 years of age was -1.2 ± 1.2 and 25.8 % (n=65) were stunted.

Nearly half of the mothers were between 20 and 24 years (n=115, 43.4%). Nearly two third of mothers had attended primary school as their highest educational level (n=167, 62.3%), whereas more than half of the fathers had primary school as the highest (n=153, 59.1%) (**Table 1**). Concerning household possession, the majority of parents had electricity (n=258 (96.3%), radio (n=243 (90.7%)), mobile (n=196 (71.1%)) and television (n=182 (67.9)). Only 3(1%) of parents who were categorized as 5th level (richest) on wealth index do not have television while 51 (82.3%) of parents who were categorized as level one (poorest) on wealth index do not have television.

Predictors of height for age Z score at 2 years

Body composition

Separate multiple linear regression models are presented for FFM and FM. FFM at birth was associated with HAZ at 2 years in both the simple (**Table 2**) and multiple linear regression analyses (**Table 3**). When adjusted for neonatal factors (**Model 1**), FFM was associated with

HAZ at 2 years ($\beta=0.68$, 95% CI (0.06, 1.31)). After adjusting for current child milk intake, hospitalization and breast feeding at 2 years the estimate of FFM was stronger (**Model 2**). HAZ at 2 years was 0.77 higher for each additional kg FFM at birth ($\beta=0.77$, 95% CI (0.13, 1.41)). Adjusting for maternal age, parental education further increased the estimate of FFM (**Model 3**) ($\beta=0.85$, 95% CI (0.20, 1.42)). Further adjustment for parental wealth index in model 4, reduced the estimate of FFM though the associations with birth body composition was still significant ($\beta=0.73$, 95% CI ((0.08, 1.38))). FM was not associated with HAZ at 2 years in all the four models and the direction of the non significant relation was negative with HAZ. The association between FFM and HAZ was not modified by sex and wealth index ($P > 0.05$).

The association between FFM at birth and HAZ at 2 years of age was also examined by excluding length at birth from the model. Unadjusted for length, the association between FFM at birth and HAZ at 2 years was stronger and highly significant (**data not shown**).

Further, in the absence of FFM and FM, association between birth weight and HAZ at 2 years was examined. However, birth weight was significant only in simple linear regression whereas it lost significance when adjusted for potential confounders in subsequent models (**data not shown**).

In addition, we have analyzed BMI z-score with HAZ at 2 years in the absence of FFM and FM. BMIZ score was positively associated with HAZ at 2 year in simple linear regression and lost significance when adjusted for potential confounders in subsequent models (**data not shown**).

In addition to FFM, in the fully adjusted model, being female was associated with 0.61 higher HAZ at 2 years ($\beta=0.61$, 95% CI (0.33, 0.89)). Each cm in length at birth was associated with

0.12 ($\beta=0.12$, 95% CI (0.01, 0.22)) larger HAZ at 2 years. A month increase in child age at 2 year was associated with a 0.24 lower in HAZ ($\beta = -0.24$, 95% CI (-0.41,-0.07)). These associations were maintained in all models (**data not shown**). HAZ was higher in children who received on cow's milk everyday compared with those who did not during the previous seven days ($\beta= 0.42$, 95%CI (0.11, 0.73)). This association was maintained in the succeeding model but not in the final model where we adjusted for parental wealth index. Higher parental wealth index score was also positively associated with HAZ ($\beta =0.14$, 95% CI (0.03, 0.26)).

Discussion

FFM but not FM was consistently positively associated with HAZ at 2 years. This association was independent of length at birth and parental wealth.

Although no previous studies have explored the relationship between birth body composition and HAZ, a number of earlier studies had identified low birth weight as a predictor of linear growth (10,15). We found that FFM rather than FM accretion during gestation might explain the association between birth weight and HAZ at 2 years of age. A higher FFM at birth might indicate healthy nutritional intake of the mother during pregnancy, which in turn may have positive effects on fetal growth and newborn health.

Barker et al has proposed that poor fetal nutrition could reduce the concentration of insulin like growth factor type 1 (IGF-1) and thereby undermine the growth of muscle mass (26). Thus, a lower concentration of IGF-1 could be one explanation why we find in the present study that reduced birth weight is particularly related to reduced FFM. A few other studies have indicated that poor growth during fetal life and infancy could permanently constrain FFM which could adversely affect later growth (27,28). There are a few studies showing that low FFM in early life predicts insulin resistance (29,30). Maternal dietary restriction may affect fetal growth directly via placental nutrient availability (31), and also indirectly via the fetal endocrine system and epigenetic modulation of gene expression (32,33).

In our study, FM at birth was not associated with HAZ at 2 years in univariate as well as multivariable analysis. However, the direction of the relationship with HAZ was negative. It is likely that fat stores at birth might represent a store of energy to fund infant growth; but we did

not find any association. Though FM was not associated with HAZ in the current study, a study conducted by Carberry *et al* in Australia showed that body fat percentage was a better predictor of neonatal morbidity than birth weight percentiles and performed better in identifying undernourished neonates (34). However, using body fat percentage as an indication of fat mass properties is not advisable since the fat percentage includes both the properties of fat mass and total body mass in the same measurement (17).

FFM and FM have distinct growth patterns during gestation. FFM accretion occurs all the way through pregnancy while more than 90% of the FM accretion occurs during late gestation and shows an accelerated growth (35). This difference in fetal tissue accretion might explain the association between FFM and HAZ as well for lack of association between FM and HAZ.

Though reference values of FFM and FM are useful in a clinical setting and field survey, in recent years few studies have provided population specific reference data. In fact, in 2013 reference data was published based on a subsample of the population included in the current manuscript(19) and the progression in development of widely applicable reference data was described (36). However, as opposed to weight and height there is no globally applicable standard available from WHO for FM and FFM.

We have also examined the association between birth weight and HAZ at 2 years. However, birth weight lost significance when adjusted for potential confounders in subsequent models. Similarly, association between BMI z score at birth and HAZ at 2 year was examined. However, BMI z score at birth lost significance when adjusted for potential confounders in the subsequent models. These finding shows the importance of using FFM and FM measurements rather than a simpler anthropometric measure like birth weight and BMI Z score. A study conducted by

Andersen et al, in the same cohort, showed a marked variation in FM and FFM for a child with the same birth weight (18). This finding indicates that studies using crude measurement techniques like body weight might miss the potential effects of variation in body composition on health outcomes.

Most of previously identified correlates were also showed statistical significant association with HAZ. In this study, female sex, birth length and parental wealth had positive association with HAZ whereas child age had negative association. Females had higher HAZ at 2 years which is corroborated by previous studies conducted in Indonesia, Bangladesh, Bhutan, and India (37,38) and meta analysis of studies from sub Saharan Africa (39).

In our study, length at birth was positively associated with HAZ at 2 years. This observation is consistent with previous study conducted in Amazon, Brazil (16), and a review from five cohort studies in low and middle income countries (40). The finding implies that length at birth is an important predictor of linear growth, revealing its importance for interventions to address intrauterine growth failure. Nevertheless, FFM at birth predicted HAZ at two years independent of birth length.

Furthermore, HAZ at 2 year was significantly higher in children from higher parental wealth index score. This finding is consistent with previous studies conducted in Bhutan Eastern Himalayas and India (37,38).

Our study has limitations. Maternal pre-pregnancy and pregnancy-related factors were not assessed. Potential confounding by complimentary feeding was also not addressed. The sample size was relatively small and might result in low statistical power. Information related to hospital

admission could have been subject to recall bias. Further, Crude measure of morbidity was used and cannot adjust well for less serious morbidities although they contribute a lot for growth faltering. Considerable loss to follow up is also a limitation. However, children included in the analyses were not statistically different from those who were not included with respect to sex, age, birth order, length, FFM and FM at birth, parental education and parental wealth index (**Supplemental Table S1**). Functional anomalies were not assessed which could potentially confound the association between BC and height. Among the main strengths of the study is it's a prospective longitudinal design, the use of an air displacement plethysmograph to assess body composition at birth which is a precise and accurate method for assessing fat and fat free mass in infants (23).

In conclusion, our study suggests that FFM at birth was associated with HAZ at 2 years. In contrast, birth FM was not a correlate of HAZ at two years of age. This finding is relevant for future research studies that are using birth weight as the outcome. It suggests that future health interventions may have greatest benefit for child growth if they improve FFM rather than FM during fetal life.

We recommend studies to better understand which part of the FFM mediates this association. Studies looking at body composition with height by including maternal pre pregnancy and pregnancy related factors in detail might be needed. Follow up studies might be required to explore how early infant body composition growth pattern are associated with linear growth. Furthermore, additional studies are required to explore how early life body composition is related to later under nutrition, childhood obesity and later non-communicable disease.

Acknowledgments

Our sincere thanks go to supervisors, research nurses and respondents and Jimma University Specialized hospital. We would like to Jimma University for giving us permission to conduct the study and publish the result.

Reference

1. Black RE, Allen LH, Bhutta ZA, et al. Maternal and child undernutrition: global and regional exposures and health consequences. *Lancet* 2008;371(9608):243–60.
2. Research Institute (IFPRI) IFP. Global Nutrition Report 2016 From Promise to Impact Ending Malnutrition by 2030. Washington, DC: International Food Policy Research Institute; 2016 . Available from: <http://ebrary.ifpri.org/cdm/ref/collection/p15738coll2/id/130354>. Accessed on September 1, 2016
3. Central Statistical Agency [Ethiopia]. Ethiopia Mini Demographic and Health Survey 2014. Addis Ababa, Ethiopia. 2014. Available at: <http://www.measuredhs.com/pubs.pdf>. Accessed on august 19, 2015
4. Black RE, Victora CG, Walker SP, et al. Maternal and child undernutrition and overweight in low-income and middle-income countries. *The Lancet* 2013;382(9890):427–51.
5. Dewey KG, Begum K. Long-term consequences of stunting in early life. *Matern Child Nutr* 2011;7:5–18.
6. Allen L, Gillespie S. What works?: a review of the efficacy and effectiveness of nutrition interventions. Geneva: United Nations, Administrative Committee on Coordination, Sub-Committee on Nutrition; 2001.
7. Bhutta ZA, Salam RA. Global Nutrition Epidemiology and Trends. *Ann Nutr Metab* 2012;61(s1):19–27.

8. Prendergast AJ, Humphrey JH. The stunting syndrome in developing countries. *Paediatr Int Child Health* 2014;34(4):250–65.
9. Iannotti LL, Zavaleta N, León Z, Caulfield LE. Growth and body composition of Peruvian infants in a periurban setting. *Food Nutr Bull* 2009;30(3):245–53.
10. Padonou G, Le Port A, Cottrell G, et al. Factors associated with growth patterns from birth to 18 months in a Beninese cohort of children. *Acta Trop* 2014;135:1–9.
11. Wells JCK. Measuring body composition. *Arch Dis Child* 2005;91(7):612–7.
12. Dencker M, Wollmer P, Karlsson MK, Lindén C, Andersen LB, Thorsson O. Body fat, abdominal fat and body fat distribution related to cardiovascular risk factors in prepubertal children. *Acta Paediatr* 2012;101(8):852–7.
13. Gishti O, Gaillard R, Durmus B, et al. Body mass index, total and abdominal fat distribution and cardiovascular risk factors in school-age children. *Pediatr Res* 2015; Available from: <http://www.nature.com.ep.fjernadgang.kb.dk/pr/journal/vaop/naam/abs/pr201529a.html> (doi:10.1038%2Fpr.2015.29). Accessed on November 9,2016
14. Hanieh S, Ha TT, De Livera AM, et al. Antenatal and early infant predictors of postnatal growth in rural Vietnam: a prospective cohort study. *Arch Dis Child* 2015;100(2):165–73.
15. Medhin G, Hanlon C, Dewey M, et al. Prevalence and predictors of undernutrition among infants aged six and twelve months in Butajira, Ethiopia: The P-MaMiE Birth Cohort. *BMC Public Health* 2010;10:27.

16. Lourenço BH, Villamor E, Augusto RA, Cardoso MA. Determinants of linear growth from infancy to school-aged years: a population-based follow-up study in urban Amazonian children. *BMC Public Health* 2012;12(1). Available from: [http://bmcpublichealth.biomedcentral.com/articles\(doi:10.1186%2F1471-2458-12-265\)](http://bmcpublichealth.biomedcentral.com/articles(doi:10.1186%2F1471-2458-12-265)). Accessed on August 8,2016
17. Wells JC. A critique of the expression of paediatric body composition data. *Arch Dis Child* 2001;85(1):67–72.
18. 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(5):501–6.
19. Andersen GS, Girma T, Wells JC, et al. 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(4):885–94.
20. World Health Organization. *Training Course on Child Growth Assessment*. Geneva, WHO,. 2008. Accessed on April 11, 2016
21. WHO Multicentre Growth Reference Study Group: *WHO Child Growth Standards: Length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age: Methods and development*. Geneva, World Health Organization. 2006. Accessed on August 9, 2016

22. Urlando A, Dempster P, Aitkens S. A New Air Displacement Plethysmograph for the Measurement of Body Composition in Infants. *Pediatr Res* 2003;53(3):486–92.
23. 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(1):90–5.
24. Lorey J. zscore06: Stata command for the calculation of anthropometric z-scores using the 2006 WHO child growth standards <http://www.stata.com/statalist/archive/2011-04/msg01386.html>. 2011. Accessed on August 31, 2015
25. Arimond M, T.Ruel M. International Food Policy Research Institute report: Progress in developing an infant and child feeding index: an example using the Ethiopia demographic and health survey 2000. 2002. Accessed on March 19, 2016
26. Barker DJ, Bull AR, Osmond C, Simmonds SJ. Fetal and placental size and risk of hypertension in adult life. *BMJ* 1990;301(6746):259–62.
27. Wells JCK. The programming effects of early growth. *Early Hum Dev* 2007;83(12):743–8.
28. Longo S, Bollani L, Decembrino L, Di Comite A, Angelini M, Stronati M. Short-term and long-term sequelae in intrauterine growth retardation (IUGR). *J Matern Fetal Neonatal Med* 2013;26(3):222–5.
29. Joglekar CV, Fall CHD, Deshpande VU, et al. Newborn size, infant and childhood growth, and body composition and cardiovascular disease risk factors at the age of 6 years: the Pune Maternal Nutrition Study. *Int J Obes* 2007;31(10):1534–44.

30. Burrows R, Correa-Burrows P, Reyes M, Blanco E, Albala C, Gahagan S. Healthy Chilean Adolescents with $\text{HOMA-IR} \geq 2.6$ Have Increased Cardiometabolic Risk: Association with Genetic, Biological, and Environmental Factors. *J Diabetes Res* 2015;2015:1–8.
31. Thornburg K, O’Tierney P, Louey S. The placenta is a programming agent for cardiovascular disease. *Placenta* 2010;31(Suppl):S54–9.
32. Jansson T, Powell TL. Role of the placenta in fetal programming: underlying mechanisms and potential interventional approaches. *Clin Sci* 2007;113(1):1–13.
33. Gabory A, Attig L, Junien C. Developmental programming and epigenetics. *Am J Clin Nutr* 2011;94(6 Suppl):1943S–1952S.
34. Carberry AE, Raynes-Greenow CH, Turner RM, Askie LM, Jeffery HE. Is body fat percentage a better measure of undernutrition in newborns than birth weight percentiles? *Pediatr Res* 2013;74(6):730–6.
35. Haggarty P. Placental regulation of fatty acid delivery and its effect on fetal growth--a review. *Placenta* 2002;23 Suppl A:S28-38.
36. Wells JCK. Toward Body Composition Reference Data for Infants, Children, and Adolescents. *Adv Nutr Int Rev J* 2014;5(3):320S–329S.
37. Aguayo VM, Badgaiyan N, Paintal K. Determinants of child stunting in the Royal Kingdom of Bhutan: an in-depth analysis of nationally representative data: Determinants of child stunting in Bhutan. *Matern Child Nutr* 2015;11(3):333–45.

38. Aguayo VM, Nair R, Badgaiyan N, Krishna V. Determinants of stunting and poor linear growth in children under 2 years of age in India: an in-depth analysis of Maharashtra's comprehensive nutrition survey: Child stunting in Maharashtra, India. *Matern Child Nutr* 2016;12:121–40.
39. Wamani H, Åstrøm AN, Peterson S, Tumwine JK, Tylleskär T. Boys are more stunted than girls in Sub-Saharan Africa: a meta-analysis of 16 demographic and health surveys. *BMC Pediatr* 2007; 14];7(1). Available from: <http://bmcpediatr.biomedcentral.com/articles> (doi:10.1186/1471-2431-7-17). Accessed on August 14, 2016
40. Stein AD, Wang M, Martorell R, et al. Growth patterns in early childhood and final attained stature: Data from five birth cohorts from low- and middle-income countries. *Am J Hum Biol* 2010;22(3):353–9.

Table 1. Child and parental birth characteristics of 268 Ethiopian study participants

Variable	Mean ± SD or n (%)
Birth characteristics	
Weight, kg	3.1 ± 0.4
Low Birth weight (<2.5kg), (%)	20.0 (7.5)
Length, cm	49.2 ± 1.9
Fat mass, kg	0.2 ± 0.2
Fat free mass, kg	2.8 ± 0.3
Female sex, (%)	135 (50.4)
Parental characteristics at birth	
Age of mother, years	23.9 ± 4.5
Maternal educational status, (%)	
No school	22 (8.2)
Primary school	167 (62.3)
≥Secondary	79 (29.5)
Paternal educational status, (%)	
No School	8 (3.2)
Primary school	153 (59.1)
≥Secondary	98 (37.8)

¹All data were obtained within 48 hours after delivery during the infants' birth examination

² The numbers in this table indicate mean± SD or Frequency (%)

Table 2: Univariate linear regression analysis between birth body composition and other covariates and child height-for-age z scores at 2 years of age in 268 Ethiopian children

	β (95% CI)	P-value
Birth characteristics		
FFM, kg	1.16 (0.72, 1.61)	<0.001*
FM, kg	1.01 (0.13, 1.88)	0.02 [†]
Length, cm	0.22 (0.15, 0.29)	<0.001*
Female sex (n=135)	0.35 (0.07, 0.63)	0.01 [†]
Child characteristics		
7-day cow milk intake		
Not at all (n=135)	Ref	
1-6 days (n=31)	0.26 (-0.19, 0.71)	0.25
Every day (n=101)	0.61 (0.31, 0.91)	<0.001*
Hospitalization since birth, Yes (n=30)	-0.38 (-1.82, 0.07)	0.10
Breast feeding at 2 years, Yes (n=169)	-0.12 (-0.42, 0.17)	0.42
Parental factors		
Maternal age at delivery, year	0.02 (-0.01, 0.05)	0.29
Maternal education		
No education (n=22)	Ref	
Primary (n=167)	0.63 (0.11, 1.15)	0.01 [†]
Secondary (n=79)	0.89 (0.35, 1.45)	0.001*
Paternal education		
No education (n=8)	Ref	
Primary (n=153)	1.01 (0.19, 1.84)	0.02 [†]
Secondary (n=98)	1.29 (0.45, 2.13)	0.003*
Parental wealth index score	0.27 (0.17, 0.37)	<0.001*

Data are given as regression coefficients (β) and 95% confidence limits.

* $p < 0.01$, significant values

[†] $p < 0.05$, significant values

Table 3: Multiple linear regression analysis examining the independent associations between birth fat free mass and fat mass on child height-for-age z score at 2year of age

	β (95% CI)			
	Model-1 ^a	Model-2 ^b	Model-3 ^c	Model-4 ^d
Fat- free mass (kg)	0.68 (0.06,1.31) †	0.77 (0.13,1.41) †	0.85 (0.20,1.50) †	0.73 (0.08,1.38) †
Fat mass (kg)	-0.18 (-1.07,0.72)	-0.41 (-1.31,0.50)	-0.46 (-1.38,0.47)	-0.45 (-1.37,0.47)

a) Newborn measurements (FFM or FM, length at birth, sex of the child) and child age at 2year

b) Model 1 + 2 years' measurements (cow milk intake at 2 year, breastfeeding at 2 year, hospitalization since birth)

c) Model 2 + parental characteristics (baseline maternal age, maternal education and paternal education)

d) Model 3 + parental wealth index

Data are given as regression coefficients (β) and 95% confidence limits. This table shows a result of two separate analyses for FFM and FM

R^2 is 0.20 for model 1, 0.22 for model 2, 0.26 for model 3 and 0.28 for model 4for the FFM model

R^2 is 0.16 for model 1, 0.18 for model 2, 0.21 for model 3 and 0.23 for model 4for the FM model

† $p < 0.05$, significant values

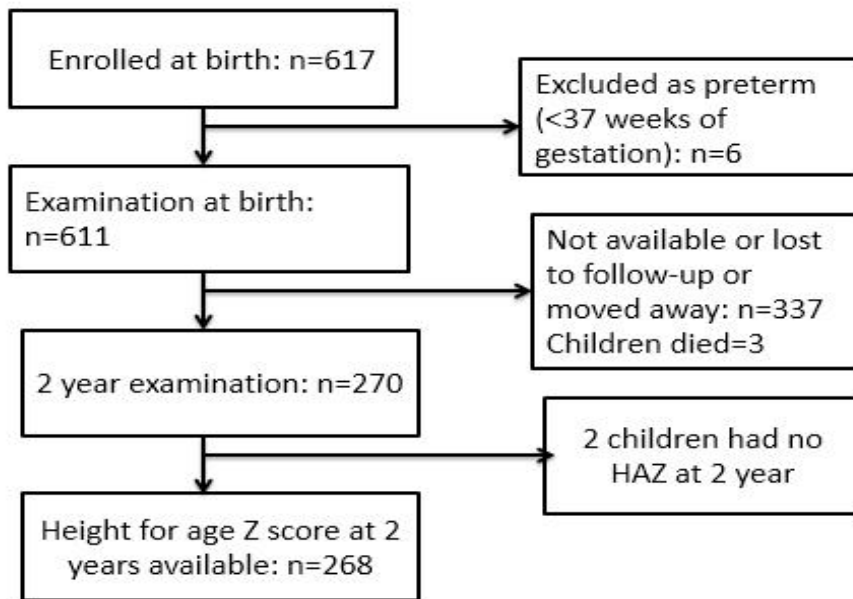


Figure 1: Flow chart of study participants

Supplemental Table S1: Comparison between children included in the analysis and lost to follow up

	Analyzed (n=268)	Lost to follow up (n=343)	P value
Birth characteristics			
Length, cm	49.2 ± 1.9	49.0 ± 2.1	0.17
FFM, kg	2.8 ± 0.3	2.8 ± 0.4	0.11
FM, kg	0.2 ± 0.2	0.2 ± 0.2	0.78
Birth weight, kg	3.1 ± 0.4	3.0 ± 0.4	0.15
Female sex, (%)	135 (50.4)	168 (48.9)	0.19
Birth order, (%)			
1 st	133 (50.2)	173 (51.6)	0.70
2 nd	65 (24.5)	88 (26.3)	
3 rd	67 (25.3)	74 (22.1)	
Maternal education at birth, (%)			
No education	22 (8.2)	22 (6.5)	0.49
Primary	167 (62.3)	201 (59.5)	
Secondary	79 (29.5)	115 (34.0)	
Parental wealth index, (%)			
1 st (poorest)	62 (23.1)	88 (25.7)	0.09
2 nd	73 (27.2)	80 (23.4)	
3 rd	49 (18.3)	54 (15.8)	
4 th	50 (18.7)	67 (19.6)	
5 th (richest)	34 (12.7)	53 (15.5)	