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Early Life Antibiotic Exposure Is Not Associated with Growth in Young Children of Vellore, India

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Abstract

Objectives—To estimate the effects of antibiotic exposures in the first 6 months of life on short- and long-term growth.

Study design—In a prospective observational cohort study of 497 children from Vellore, India, we estimated short-term effects of antibiotics during the first 6 months using longitudinal general linear regression to model weight-forage, height-for-age, and weight-for-height z-scores in monthly intervals. To estimate long-term effects, we modeled growth from 6 months to 3 years as a function of antibiotic use in the first 6 months. We also estimated the effects of antibiotics on the monthly relative risks of underweight, stunting, and wasting in the first 6 months and to 3 years.

Results—Underweight, stunting, and wasting were common in this population: 31%, 32%, and 15% on average after 6 months of age, respectively. There was no association between antibiotic exposures before 6 months and growth during that period. From 6 months to 3 years, adjusted absolute differences in weight and height were small (approximately −100 g and no more than −2 mm overall, respectively) and not statistically significant.

Conclusions—Antibiotic exposures early in life were not associated with increased or decreased growth. The combination of malnutrition and recurrent illness likely complicate the relationship between antibiotic exposures and growth among children in low and middle-income countries.

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In an era of concern over the growing obesity epidemic in developed countries, antibiotic exposures early in life have been recently identified as a potential contributor to excessive weight gain.[1,2] This hypothesis originated from the clear growth-promoting effects of antibiotics in livestock when given long-term and in subtherapeutic dose.[3] Although the biological mechanism is largely unknown, it is hypothesized that antibiotics affect growth through interaction with the gastrointestinal microbiota,[3,4] which plays an important role in supporting nutrient absorption and other metabolic functions.[5,6] Several epidemiologic studies among children in high-income countries have supported this hypothesis, finding associations between antibiotic use early in life and increased risk for obesity in later childhood.[7-9]

In low and middle-income countries (LMICs), this potential relationship is complicated by the high prevalence of malnutrition and recurrent illnesses that can cause major height and weight shortfalls.[10,11] Subclinical infections associated with living in unhygienic environments are associated with environmental enteropathy, which results in impaired function and structure of the small intestine and reduces nutrient absorption.[12-4] For children with severe acute malnutrition, antibiotics are recommended to treat and prevent subclinical infections in an effort to improve recovery.[15,16] In several studies, acutely malnourished children who received antibiotics showed improved recovery rates, lower mortality, and in some cases improved weight gain compared with children receiving nutritional supplements alone.[16-18]

However, as our group showed recently, antibiotics may also increase risk for diarrhea,[19,20] which is associated with poor growth and can contribute to the synergism between infections and growth failure.[21] Therefore, it is unclear what the net impact of antibiotic treatment for common childhood illnesses may be among children in low-income settings.

We aimed to estimate the effect of antibiotic use before 6 months of age on short-term (within the first 6 months) and long-term (up to 3 years of age) growth in an observational birth cohort from Vellore, India. We focused on antibiotic use in the first 6 months because antibiotics have the largest impact on the developing microbiota[2,22,23] and subsequent diarrhea at this age,[19] and we expect this exposure period to correspondingly have the largest effects on growth, as previously shown.[7]

Methods

We analyzed data from a prospective observational cohort study of immune responses to cryptosporidiosis in 497 children from semi-urban slums of Vellore, India from 2009-2013. The study population, enrollment strategy, and data collection methods have been previously described.[24] Briefly, baseline information on demography, socioeconomic indicators, environment, and delivery characteristics were collected at enrollment. Fieldworkers interviewed caregivers twice per week from birth to 3 years of age about all illnesses since the last visit and further recorded details of diarrhea severity, hospitalization, and treatments given. Diarrhea was defined using the standard World Health Organization (WHO) definition as at least 3 loose or watery stools in a 24-hour period,[25] and severity was assessed by the Vesikari scale.[26]

Antibiotic exposure was defined in monthly intervals as antibiotic use for any illness. Children were considered exposed either if a caregiver reported antibiotic use for diarrhea during home visits by fieldworkers or if a prescription for antibiotics was recorded in study clinic records for any illness (including diarrhea). We excluded all topical antibiotics.

Height and weight were measured each month of follow-up at the study clinic using single measurements. Weight was measured using a Salter weighing scale to the nearest 100 g. Recumbent length was measured using a standard infantometer for the first year of life, and subsequently height was measured with a stadiometer, both to the nearest millimeter. Biologically implausible height and weight values were discarded, and we considered measurements taken within 1 week before or after a child's monthly birth anniversary as their weight/height at that month of age. Written informed consent was obtained from the parents or guardians of the participating children. The study was approved by the Institutional Review Boards of the Christian Medical College (Vellore, India), Tufts University Health Sciences (Boston, Massachusetts), and University of North Carolina (Chapel Hill, North Carolina).

We used the 2006 WHO child growth standards[27] as the reference population to calculate weight-for-age (WAZ), height-for-age (HAZ), and weight-for-height (WHZ) z-scores. Children were classified as underweight (WAZ < −2 SD from the growth reference), stunted (HAZ < −2 SD), and/or wasted (WHZ < −2 SD). We also translated the effects on z-scores to their equivalents in absolute height and weight using the age and sex-specific SD differences in weight/height from the WHO expanded z-score tables.[28,29]

Because the proportion of missing data was 3% or less for all baseline variables, we imputed the median values of baseline variables for individuals with missing data.

Data Analyses: Short-Term Effects

We used longitudinal general linear regression to model WAZ, HAZ, and WHZ at monthly intervals from 0-5 months of age. Specifically, we estimated the effects of antibiotic exposures in a given month on WAZ, HAZ, and WHZ at the end of the following month (Figure 1, A; available at www.jpeds.com), and accounted for correlation between outcomes from the same child using generalized estimating equations (GEE) with a robust variance estimator. This model structure allowed for a 1 month lag between antibiotic exposure and the measurement of growth outcomes. To assess the sensitivity of results to this lag period, we repeated the analyses with outcomes both at the end of the same month as the exposure, as well as at 2 months following the exposure month (Figure 1, B and C).

Confounding variables for the exposure model were chosen a priori by causal directed acyclic graph[30] to account for determinants of antibiotic use which also affect child growth, including growth status before exposure, other base-line characteristics, and illness burden. These variables were included to isolate the effects of antibiotics from the under-lying conditions for which they were given. Optimal variable coding was determined by the Quasi-likelihood under the Independence model Criterion, which is appropriate for GEE models.[31]

The final models included child sex, socioeconomic status (based on the modified Kuppuswamy scale[32]), maternal education, household hygiene,[33] household crowding, low birth weight (<2.5 kg), preterm birth (<37 weeks of gestation), cesarean delivery, and characteristics of the exposure month: growth z-score at the beginning of the month, exclusive breastfeeding, number of days with infections and severe illnesses, number of days with diarrhea, severe diarrhea episodes (Vesikari score[26] ≥ 11), prolonged or persistent diarrhea episodes (≥7 days), dehydration during diarrhea, oral rehydration solution given during diarrhea, hospitalization, and days with diarrhea in the previous month. We separately stratified effects using interaction terms by month of antibiotic exposure, sex, exclusive breastfeeding in the exposure month, baseline malnutrition status (underweight, stunted, or wasted), and illness burden.

To validate our results with an alternate model that eliminates potential unmeasured child-level confounding, we used a fixed-intercept model in which the effects of antibiotic use in monthly intervals were estimated within-child (a child's exposed and unexposed months served as the index and reference exposures, respectively).[34] We used the robust variance estimator to account for correlation between observations within-child and necessarily included only the time-varying covariates[34] listed above.

Data Analyses: Long-Term Effects

We created descriptive height and weight growth curves after 6 months of age by grouping measurements by month and averaging heights and weights across children given the same number of antibiotic courses before 6 months.

We then used longitudinal general linear regression with GEE to model all WAZ, HAZ, and WHZ after 6 months of age as a function of antibiotic use in the first 6 months. We included the corresponding growth z-score at 6 months in the models to account for differences in growth occurring prior to and during the antibiotic exposure period; this ensured estimation of long-term effects on growth rates following 6 months of age. Baseline confounding variables included all those in the short-term analysis. Indicators of illness burden were summarized over the first 6 months as total number of days with diarrhea, infections, and severe illnesses, maximum Vesikari score[26] of diarrhea episodes, prolonged or persistent diarrhea episodes, and fever or dehydration during diarrhea, and exclusive breastfeeding at 3 months. We stratified effects by sex, number of antibiotic courses received before 6 months, and age period of growth (6 months-1 year, 1-2 years, 2-3 years). We further assessed modification of effects by exclusive breastfeeding, illness burden, and malnutrition status at 6 months.

We estimated the effects of antibiotics on the relative risks of underweight, stunting, and wasting in both the short and long-term with the same exposure groups and covariates as the linear regression models. We used longitudinal Poisson regression with the robust variance estimator as an approximation of log-binomial regression[35] because the logbinomial models did not converge.

We validated results by repeating analyses with a more specific, but less sensitive, definition of antibiotic exposure, which required the caregiver to list a confirmed antibiotic name for diarrhea instead of only replying “yes” when asked if antibiotics were given.

Results

The birth cohort consisted of 497 children, 456 (91.8%) of whom remained in the study and were measured at least once after 6 months of age. In the remaining study period, 46 (9.3%) more children were lost to follow-up. Nine drop-outs were due to death. The majority of participants were from families of low socioeconomic status with poor household hygiene and crowding in the home (Table I).

More than one-half of children (n = 262, 57.5%) were exposed to antibiotics by 6 months of age, and 137 (28.1%) had received more than 1 course (Figure 2, A). Antibiotic use was highest from 3-5 months of age, with an average monthly exposure prevalence of 20.3%.

Growth failure early in life was common (Figure 2, B). By 6 months, on average 30.6% of children were underweight (maximum prevalence 40.7% at 27 months) and 31.8% of children were stunted (maximum prevalence 34.7% at 32 months). Prevalence of wasting (WHZ < −2 SD) was lower, at 15.0% overall.

Short-Term Antibiotic Effects

Averaged across months from birth through 5 months, there was no crude difference in WAZ or WHZ associated with antibiotic exposure in a given month (WAZ difference: 0.01, 95% CI: −0.05, 0.06; WHZ difference: 0.05, 95% CI: −0.04, 0.14). These effects were uniform by sex. Conversely, antibiotic use was crudely associated with slightly lower HAZ (HAZ difference: −0.12, 95% CI: −0.19, −0.06); this effect was more pronounced among girls (HAZ difference: −0.17, 95% CI: −0.26, −0.07) than boys (HAZ difference: −0.09, 95% CI: −0.17, 0.00).

After multivariable adjustment, the absence of effects on WAZ and WHZ remained. The effect on HAZ was no longer significant and moved toward the null, entirely for boys and reduced by more than one-half among girls (Table II). The adjusted weight and height differences among boys translated to a difference of −1 g and −0.1 mm, respectively. Among girls, the effects corresponded to differences of −32 g and −1.2 mm. Effects were largest for exposures in the first month of life but were imprecise due to few exposed children (n = 30). There was no statistically significant effect modification by month (*P* for heterogeneity = .7; Table III available at www.jpeds.com), malnutrition status of the child (underweight, stunted, or wasted), exclusive breastfeeding, diarrhea burden, or other infections and severe illness burden (results not shown).

There was also no difference in the relative risks of underweight or wasting among children who received antibiotics compared with those who did not (Table II). However, girls who received antibiotics in a given month had a higher risk of being stunted in the next month (risk ratio: 1.27, 95% CI: 1.04, 1.56). There was no effect on stunting among boys.

Long-Term Antibiotic Effects

For the analysis of the effect of antibiotics before 6 months of age on growth from 6 months to 3 years, a total of 12 694 growth measurements were available among 456 children remaining in the study at 6 months (mean of 27.8 measurements/child). The majority of children (n = 388, 85.1%) had at least 29 growth measurements before 3 years of age.

Crude average growth curves after 6 months of age stratified by sex and early life antibiotic exposure are shown in Figure 3. Children receiving no or one course of antibiotics had similar growth trajectories, and those receiving 2 or more courses of antibiotics weighed less and were shorter at all ages. Correspondingly, there was a crude negative association of antibiotic use in the first 6 months on WAZ (difference: −0.18, 95% CI: −0.35, −0.02) and HAZ (difference: −0.20, 95% CI: −0.38, −0.02) from 6 months to 3 years of age.

Adjusted effects were smaller in magnitude and no longer statistically significant, but still negative, such that antibiotic use before 6 months of age was associated with lower WAZ, HAZ, and WHZ after 6 months (Table II). The associations were largest after 1 year of age (*P* for heterogeneity <.0001). There was no evidence for a difference in effect by sex or number of antibiotic courses received (*P* for heterogeneity >.4). All effects were minimal when translated to weight and height differences. The largest differences in weight (occurring at 2-3 years of age) corresponded to approximately −150 g. The largest differences in height were −3.1 mm from 2-3 years, and the difference was −1.5 mm overall. There was no significant effect modification by burden of illnesses, hospitalization, baseline malnutrition status, or exclusive breastfeeding (results not shown).

There was an increase in the relative risk of underweight after 6 months of age among children who received antibiotics in the first 6 months compared with children who did not receive antibiotics (risk ratio: 1.33, 95% CI: 1.07, 1.64; Table II). The risk of wasting was also elevated, but the estimates were not statistically significant. There were no effects on long-term stunting.

Sensitivity Analyses

The effects of antibiotics in a given month were not sensitive to the time period between the antibiotic exposure and outcome (Figure 1, B and C and Table IV; Table IV available at www.jpeds.com). Results from the fixed-intercept model, which eliminated potential unmeasured child-level confounding, were qualitatively and quantitatively similar to results from the general linear models (Table V; available at www.jpeds.com). Using an alternative definition of exposure, which required the caregiver to list a confirmed antibiotic name, there was no change in short- or long-term effects (results not shown).

Discussion

Our study provides evidence from a prospective observational cohort study concerning the impact of early life antibiotic exposures on growth among LMIC children. Unlike other investigations of the relationship between antibiotics and growth, we did not find evidence that antibiotic exposures early in life were associated with growth promotion. Antibiotic exposures before 6 months of age did not have any short-term associations with growth, and

were associated only with small, but not statistically or clinically significant, differences in height and weight from 6 months to 3 years. These differences were near the limits of detection of the measurement instruments (approximately 100 g and 1-2 mm overall). We suggest these small negative effects on growth may be due to residual confounding or chance given the large number of comparisons made.

There are several potential explanations for the lack of a growth-promoting effect. Most of the previous studies showing increased weight gain or risk of obesity associated with antibiotics[7-9,36,37] were conducted in high-income countries with Western diets. Animal studies have shown that the growth-promoting phenotype associated with an altered microbiota is amplified when the animals are fed a high-fat diet.[2,38,39] Our study population from semi-urban slums did not have access to a high-fat diet after weaning such that an interaction between antibiotics and increased caloric intake was unlikely. Also, no children in this study were diagnosed with acute severe malnutrition, for which antibiotics have shown to improve recovery and/or growth.[17,18] Our study population was community-based, and few would have met the inclusion criteria (eg, preterm, very low birth weight, with severe illness) for the trials demonstrating improved growth associated with antibiotics.[18,38,40,41]

In LMICs, previous studies of the effects of antibiotics on growth have been inconclusive. A recent meta-analysis of 10 trials of antibiotics conducted over a 60-year period concluded that antibiotics improved growth, though the summary effect sizes were likely not clinically important (less than 1 mm/month difference in height and 24 g/month in weight).[18] An international cross-sectional study also reported that overall adjusted body mass index at age 5-8 years was higher in children exposed to antibiotics in infancy. However, the effects varied across sites and, critically, a lower in body mass index associated with antibiotics was found in all countries classified as nonaffluent except Thailand.[42]

The small association of antibiotics with lower WAZ and HAZ in the long term may be due to increased diarrheal rates following antibiotic exposure,[19] which may be associated with poor growth. However, diarrhea likely had minimal impact on growth in our study population because of high use of oral rehydration solution during diarrhea (88%), counselling to continue breastfeeding, and good access to healthcare. Therefore, appropriate treatment may have mitigated any effects increased diarrhea burden would have had on growth. It is also possible that the 2 competing pathways: antibiotics as growth-promoters and antibiotics as causing future illness and harming growth, may both have been occurring, resulting in a null net effect on growth.

Because the study was observational in design, we cannot exclude the possibility of uncontrolled confounding. Even after multivariable adjustment, we may not have been able to completely capture aspects of child illness needed to separate the effects of antibiotics from their indicating illnesses. However, a randomized clinical trial would be unethical because treatment of some illnesses with antibiotics is necessary, and our study provides results in a community-based setting that may be more generalizable to communities in LMICs.[43]

The study was also limited by potential misclassification of antibiotic exposures because of recall errors among caregivers and missed antibiotic prescriptions received outside of the study clinic for non-diarrheal illnesses. The duration of antibiotic exposures was also unknown. However, because the clinic was located within the residential area of study subjects and provided free care and medicines, we expect almost all prescriptions to have originated in the study clinic. Good concordance between caregiver-reported and antibiotic prescriptions for diarrhea supports this assumption (78% of antibiotic prescriptions during diarrhea episodes were associated with caregiver-reported antibiotic treatment). Further, our results were consistent when we used alternative definitions of antibiotic exposure in sensitivity analyses.

The combination of malnutrition and recurrent illness complicate the relationship between antibiotic exposures and growth among children in LMICs. Understanding the multifactorial impact of antibiotic use across settings is important because the majority of children in our cohort were exposed early in life, and antibiotic stewardship is vital to preventing the development of drug resistance.[44,45] Our study among children in south India did not replicate previous associations between early life antibiotic use and increased growth demonstrated among children in high-income countries and when given in combination with nutritional rehabilitation for more severely malnourished children. Conversely, antibiotic exposure in the first 6 months of life was not associated with differences in growth both during the first 6 months and up to 3 years of age.

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Glossary

GEE	Generalized estimating equations
HAZ	Height-for-age z-score
LMIC	Low and middle-income country
WAZ	Weight-for-age z-score
WHO	World Health Organization
WHZ	Weight-for-height z-score

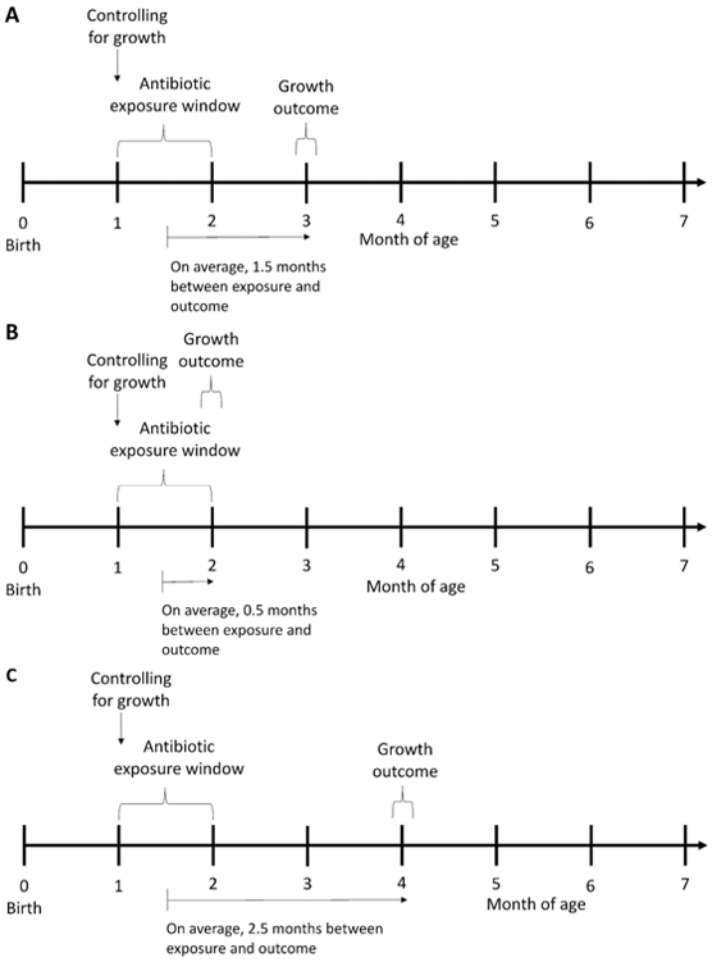

Figure 1.

Schematic of exposure period and age of outcome assessment for short-term analyses, as well as age of baseline growth measurement included in the models and the average time between exposure and growth outcome. The analyses included the analogous scheme for all months through 6 months of age. **A**, Primary analysis, and **B**-**C**, sensitivity analyses.

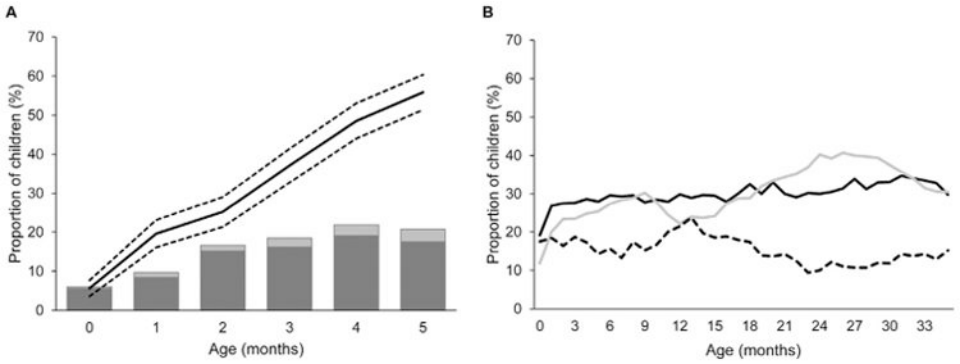

Figure 2.

A, Antibiotic exposure before 6 months of age. *Dark gray bars*, Children exposed to 1 course of antibiotics in a given month; *light gray bars*, children exposed to more than 1 course of antibiotics in a given month; *black line*, cumulative proportion of children exposed to at least one course of antibiotics (95% CI; *dotted lines*). **B**, Prevalence of underweight (*black line*), stunting (*gray line*), and wasting (*black dotted line*) from 0-3 years of age.

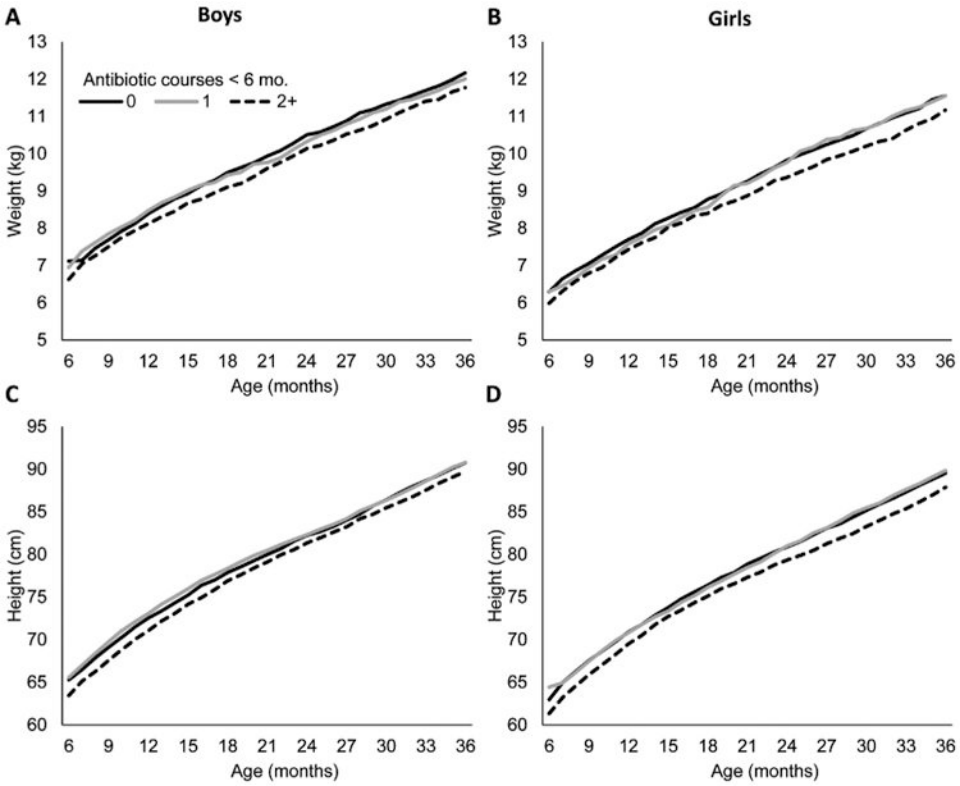

Figure 3.

Crude average weight (**A**, boys, and **B**, girls) and height (**C**, boys, and **D**, girls) growth curves by antibiotic exposure in the first 6 months of life. *Black line*, no antibiotic courses; *gray line*, 1 antibiotic course; *black dotted line*, 2+ antibiotic courses.

Table I

Demographic characteristics

	No. children (%)
Household characteristics	
Socioeconomic status *	
Low	328 (66.0)
Medium	160 (32.2)
High	9 (1.8)
Maternal education	
No formal education	184 (37.0)
Primary/middle school	167 (33.6)
Higher secondary school	129 (26.0)
College/polytechnic/professional school	17 (3.4)
Poor household hygiene †,‡	256 (53.5)
Crowding	
High (>4 people/room)	164 (33.0)
Medium (>3-4 people/room)	190 (38.2)
Low (≤3 people/room)	143 (28.8)
Child characteristics	
Sex of child	
Male	263 (52.9)
Female	234 (47.1)
Cesarean delivery	90 (18.1)
Low birth weight (<2.5 kg)‡	84 (17.1)
Preterm birth (<37 wk of gestation)	50 (10.3)
Antibiotics at birth‡	13 (2.7)
Age (mo) at stopping exclusive breastfeeding (mean, SD)	3.9 (2.10)
Age (mo) at stopping all breastfeeding (mean, SD)	15.9 (8.72)

* Socioeconomic status categories defined from the modified Kuppuswamy scale based on educational and occupational level of the family, house ownership, total number of rooms in the house, and household possessions.[29]

† Poor household hygiene was based on a score of less than 12 on a scale developed from an assessment of water, food, and personal hygiene.[30]

‡ Two missing observations for hygiene; 7 missing observations for low birth weight; 12 missing observations for preterm birth; 15 missing observations for antibiotics at birth.

Table II

Estimated adjusted effects of antibiotic treatment under 6 months of age on growth in the short-term (effect in 1 month on growth at the end of the following month) and long-term (from 6 months to 3 years)

	WAZ	Underweight	HAZ	Stunted	WHZ	Wasted
	β^* (95% CI)	RR† (95% CI)	β^* (95% CI)	RR† (95% CI)	β^* (95% CI)	RR† (95% CI)
Short-term effects: Any antibiotics (n = 276) vs none (n = 221) in 1-mo intervals <6 mo						
Overall effect	−0.02 (−0.08, 0.04)	0.98 (0.86, 1.13)	−0.03 (−0.10, 0.04)	1.07 (0.92, 1.23)	0.02 (−0.07, 0.12)	0.96 (0.78, 1.18)
By sex						
Males	−0.00 (−0.07, 0.08)	0.93 (0.78, 1.11)	−0.01 (−0.09, 0.10)	0.94 (0.77, 1.14)	−0.00 (−0.13, 0.13)	0.94 (0.73, 1.20)
Females	−0.05 (−0.13, 0.04)	1.07 (0.88, 1.31)	−0.06 (−0.16, 0.03)	1.27 (1.04, 1.56)	0.05 (−0.09, 0.19)	0.98 (0.72, 1.33)
Long-term effects: Any antibiotics <6 mo (n = 262) vs none <6 mo (n = 194)						
Overall effect	−0.08 (−0.19, 0.02)	1.33 (1.07, 1.64)	−0.05 (−0.17, 0.06)	1.07 (0.88, 1.31)	−0.10 (−0.23, 0.02)	1.25 (0.94, 1.67)
By sex						
Males	−0.08 (−0.23, 0.06)	1.39 (1.03, 1.87)	−0.02 (−0.18, 0.14)	1.03 (0.79, 1.35)	−0.15 (−0.32, 0.02)	1.37 (0.94, 2.01)
Females	−0.08 (−0.23, 0.06)	1.26 (0.96, 1.66)	−0.09 (−0.24, 0.06)	1.13 (0.87, 1.47)	−0.06 (−0.22, 0.10)	1.13 (0.76, 1.69)
By courses						
1 course	−0.09 (−0.21, 0.03)	1.48 (1.16, 1.88)	−0.03 (−0.16, 0.10)	1.08 (0.85, 1.38)	−0.11 (−0.26, 0.03)	1.35 (0.98, 1.87)
2+ courses	−0.08 (−0.21, 0.05)	1.22 (0.95, 1.55)	−0.08 (−0.22, 0.06)	1.07 (0.86, 1.34)	−0.10 (−0.24, 0.05)	1.13 (0.80, 1.60)
By age						
6 mo-1 y	0.01 (−0.07, 0.08)	1.23 (0.96, 1.58)	−0.01 (−0.10, 0.08)	0.96 (0.76, 1.22)	0.01 (−0.10, 0.11)	0.94 (0.68, 1.30)
1-2 y	−0.12 (−0.24, 0.01)	1.46 (1.15, 1.87)	−0.06 (−0.18, 0.07)	1.16 (0.90, 1.49)	−0.15 (−0.30,-0.00)	1.36 (0.97, 1.89)
2-3 y	−0.11 (−0.25, 0.03)	1.25 (0.98, 1.60)	−0.09 (−0.25, 0.07)	1.07 (0.85, 1.35)	−0.12 (−0.27, 0.03)	1.37 (0.91, 2.06)

RR, risk ratio.

*Absolute change in z-score from longitudinal general linear regression models with robust variance adjusted for child sex, prior growth z-score, socioeconomic status,[32] maternal education, household hygiene,[33] household crowding, low birth weight, preterm birth, cesarean delivery, exclusive breastfeeding, infections and severe illnesses, and indicators of diarrhea severity.

†Relative risk from longitudinal Poisson regression models with robust variance (approximation of log-binomial regression) adjusted for the same covariates as above.

Table III

Stratified by month, estimated adjusted effects of antibiotic treatment in 1 month on growth at the end of the following month

		WAZ in next month	HAZ in next month	WHZ in next month
Age at exposure	**No. (%)**	**β^* (95% CI)**	**β^* (95% CI)**	**β^* (95% CI)**
None		0	0	0
0 mo	30 (6.0)	−0.28 (−0.61, 0.05)	0.05 (−0.32, 0.42)	−0.13 (−0.62, 0.35)
1 mo	48 (9.7)	−0.05 (−0.26, 0.16)	−0.10 (−0.32, 0.12)	0.11 (−0.29, 0.51)
2 mo	81 (16.6)	0.03 (−0.10, 0.16)	−0.06 (−0.22, 0.10)	0.17 (−0.06, 0.40)
3 mo	89 (18.5)	−0.01 (−0.11, 0.09)	−0.04 (−0.16, 0.09)	−0.00 (−0.17, 0.16)
4 mo	104 (21.8)	0.01 (−0.08, 0.10)	−0.06 (−0.17, 0.05)	0.01 (−0.17, 0.19)
5 mo	97 (20.7)	−0.02 (−0.14, 0.09)	0.01 (−0.12, 0.15)	−0.06 (−0.25, 0.13)

* Absolute change in z-score adjusted for child sex, previous growth z-score, socioeconomic status, maternal education, household hygiene, household crowding, low birth weight, preterm birth, cesarean delivery, exclusive breastfeeding, infections and severe illnesses, indicators of diarrhea severity, and antibiotic exposure history.

Table IV

Estimated adjusted effects of antibiotic treatment in 1 month on growth at the end of the month and at the end of the second following month

	WAZ	HAZ	WHZ
Antibiotics in exposure mo	**β^* (95% CI)**	**β^* (95% CI)**	**β^* (95% CI)**
Outcome: at end of exposure mo			
No	0	0	0
Yes			
Males	−0.03 (−0.10, 0.04)	−0.01 (−0.10, 0.09)	−0.03 (−0.16, 0.09)
Females	−0.01 (−0.09, 0.07)	−0.11 (−0.20,−0.03)	0.17 (0.04, 0.31)
Overall	−0.02 (−0.08, 0.03)	−0.05 (−0.12, 0.01)	0.05 (−0.04, 0.16)
Outcome: at end of second mo following exposure			
No	0	0	0
Yes			
Males	0.05 (−0.02, 0.12)	0.03 (−0.05, 0.12)	0.01 (−0.11, 0.12)
Females	−0.03 (−0.10, 0.04)	−0.05 (−0.14, 0.04)	0.01 (−0.12, 0.14)
Overall	0.01 (−0.04, 0.07)	−0.00 (−0.07, 0.06)	0.01 (−0.08, 0.10)

*Absolute change in z-score adjusted for child sex, previous growth z-score, socioeconomic status, maternal education, household hygiene, household crowding, low birth weight, preterm birth, cesarean delivery, exclusive breastfeeding, infections and severe illnesses, indicators of diarrhea severity, and antibiotic exposure history.

Table V

Estimated adjusted effects of antibiotic treatment in 1 month on growth at the end of the following month using the fixed-intercept model

	WAZ in next mo	HAZ in next mo	WHZ in next mo
Age at antibiotic exposure	**β^* (95% CI)**	**β^* (95% CI)**	**β^* (95% CI)**
No antibiotics	0	0	0
0-5 mo	0.02 (−0.04, 0.08)	−0.02 (−0.09, 0.05)	0.03 (−0.07, 0.12)
Males	0.05 (−0.02, 0.12)	0.02 (−0.07, 0.11)	0.00 (−0.13, 0.13)
Females	−0.01 (−0.10, 0.08)	−0.07 (−0.16, 0.02)	0.06 (−0.08, 0.20)
0-2 mo	0.02 (−0.08, 0.12)	−0.02 (−0.15, 0.11)	0.09 (−0.09, 0.27)
3-5 mo	0.01 (−0.05, 0.08)	−0.01 (−0.09, 0.07)	−0.01 (−0.12, 0.10)

*Absolute change in z-score adjusted for child sex, previous growth z-score, socioeconomic status, maternal education, household hygiene, household crowding, low birth weight, preterm birth, cesarean delivery, exclusive breastfeeding, infections and severe illnesses, indicators of diarrhea severity, and antibiotic exposure history.