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Original Contribution

Infant Growth Trajectories and Lipid Levels in Adolescence: Evidence From a Chilean Infancy Cohort

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Growth in early infancy is hypothesized to affect chronic disease risk factors later in life. To date, most reports draw on European-ancestry cohorts with few repeated observations in early infancy. We investigated the association between infant growth before 6 months and lipid levels in adolescents in a Hispanic/Latino cohort. We characterized infant growth from birth to 5 months in male ($n = 311$) and female ($n = 285$) infants from the Santiago Longitudinal Study (1991–1996) using 3 metrics: weight (kg), length (cm), and weight-for-length (g/cm). Superimposition by translation and rotation (SITAR) and latent growth mixture models (LGMMs) were used to estimate the association between infant growth characteristics and lipid levels at age 17 years. We found a positive relationship between the SITAR length velocity parameter before 6 months of age and high-density lipoprotein cholesterol levels in adolescence (11.5, 95% confidence interval; 3.4, 19.5), indicating higher high-density lipoprotein cholesterol levels occurring with faster length growth. The strongest associations from the LGMMs were between higher low-density lipoprotein cholesterol and slower weight-for-length growth, following a pattern of associations between slower growth and adverse lipid profiles. Further research in this window of time can confirm the association between early infant growth as an exposure and adolescent cardiovascular disease risk factors.

high-density lipoprotein cholesterol; infant growth; length; low-density lipoprotein cholesterol; triglycerides; weight; weight-for-length

Abbreviations: BIC, Bayesian information criterion; CI, confidence interval; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LGMM, latent growth mixture model; SITAR, superimposition by translation and rotation; SLS, Santiago Longitudinal Study; TC, total cholesterol; WFL, weight-for-length.

Following a "developmental origins of health and disease" concept, animal models and observational studies offer evidence that anthropometric growth patterns early in development influence cardiovascular risk factors. Animal models have demonstrated a link between postnatal growth or feeding conditions prior to weaning and plasma lipid outcomes, including total cholesterol (TC), triglycerides, and/or high-density lipoprotein cholesterol (HDL-C)—but with inconsistent directions of association (1–5). Despite mixed evidence, these studies suggest altered lipid levels following differential growth in offspring. Hypothesized mechanisms responsible for these associations include postnatal growth as an environmental stimulus that influences genomic expression and resultant metabolic programming (6).

Findings from prospective cohort studies also indicate that increases in weight or length in the first 1 to 2 years are associated with lipid profiles, with most indicating lower HDL-C and higher low-density lipoprotein cholesterol (LDL-C) and triglyceride levels at ages from 4 years (7, 8) to adolescence and into young adulthood (9–11). When assessing peak weight velocity, which requires at least 3 repeated measurements, there was a positive association with a favorable lipid profile (i.e., higher HDL-C and lower triglycerides) (12). Most of these observational studies focus on samples with few repeated measurements in early infancy, restricting the types of growth characterizations possible during a period of rapid change as occurs in the first 6 months of human life (13). Furthermore, these characterizations of growth in infancy do not leverage advanced methodological

approaches in assessing potential growth patterns that may best fit nonlinear trajectories. The paucity of evidence involving detailed growth characterization in early infancy motivates further study to better understand the role this early developmental period may play in lipid metabolism.

Given conflicting evidence and few observational studies containing detailed growth estimates in early infancy and their possible association with lipid profiles later in life, our aim for this study was to characterize growth during this early developmental period and to assess its association with lipid levels in adolescence. In line with most prior evidence (7–11), our hypothesis was that faster growth is associated with unfavorable lipid profiles. Results from this study can provide evidence of associations between growth in early infancy and lipid disturbances to inform potential interventions.

METHODS

Sample

The Santiago Longitudinal Study (SLS) is a cohort study that started as an infancy iron-deficiency-anemia preventive trial from 1991–1996 (14–16). The trial consisted of different types of iron supplementation randomized to groups at 6 months of age (16). Participants were recruited from low- to middle-income, working-class neighborhoods in Santiago, Chile. Inclusion criteria for the preventive trial included full-term singleton infants, vaginal births with birth weight of ≥3.0 kg, and no major health problems (i.e., congenital abnormalities), and resulted in 1,657 infants completing the study from 6 to 12 months (Web Figure 1, available at https://doi.org/10.1093/aje/kwac057). Any infant with iron deficiency anemia at 6 months was invited to be part of a neuromaturation study and, with nonanemic controls, they were not included in this sample (n = 135). A subset of SLS participants were followed into adolescence as part of a study focused on cardiovascular risk factors, including lipid profiles. To evaluate the chance for selection bias due to sample attrition, we compared sociodemographic characteristics such as gestational age, birth weight, parental education, and maternal age for the subset of adolescent participants in our analytical sample of the 596 adolescents and the group of participants who only completed the study in the first year of life, and we did not find any substantive differences between the groups (Web Table 1). This finding suggests a lack of selection bias, supported by prior findings (14, 17). For this analysis, lipid measurements collected at 16–17 years of age were the outcomes of interest (n = 596). We omitted individuals with lipid values exceeding 5 standard deviations above or below the mean (n = 6). Omitting these individuals representing the highest values of hyperlipidemia for triglycerides (n = 5) and LDL-C (n = 1) in this sample allowed for better model fit after examining residuals and, if left in the analyses, did not change interpretation of the coefficient estimates.

Anthropometric, lipid, and covariate measures

Longitudinal measurements of weight (kg), length (cm), and weight-for-length (WFL) (g/cm) measured at each month up to 6 months were used to model growth trajectories. We did not standardize these measurements because z scores can attenuate changes in anthropometric measures for larger individuals at baseline (18) and would lead to lower power and the potential for biased estimates (19). Weight was measured to the nearest 0.01 kg on an electronic scale at well-baby visits in local public health clinics (15). Length was measured on a recumbent board to the nearest 0.1 cm.

TC, HDL-C, and triglyceride values were obtained with venipuncture from participants at a median age of 16.8 years following a 12-hour overnight fast. The lipid panel was measured with a dry analytical method in the Vitros system (Ortho Clinical Diagnostics Inc., Raritan, New Jersey) (20). LDL-C was calculated using the Friedewald equation (21): TC − HDL-C − triglycerides/5. We also assessed the triglyceride:HDL ratio. We visually examined the distributions of each lipid measure and log transformed the triglyceride values to account for a skewed distribution.

Statistical methods

Summary statistics included median and interquartile range for the continuous variables and percentages with counts for categorical variables. All summary statistics were combined and stratified by sex of child.

After careful consideration of confounders in a directed acyclic graph (Web Figure 2), adjusted analyses included sex of child, gestational age, breastfeeding until 6 months, and socioeconomic status as measured by a modified Graffar index (22). This index represents socioeconomic position within lower-income countries (23), and it includes 12 measures, such as education, expenditures, and housing characteristics, which are summed to create a scale with higher values indicating lower social class. All growth measurements in this analysis precede the randomization of the iron supplement groups at 6 months (14); however, we included randomization status as a covariate.

To estimate the association between early infant growth and lipid measures, we used 2 different approaches: 1) superimposition by translation and rotation (SITAR), a nonlinear mixed effects approach (24), and 2) latent growth mixture models (LGMMs) (25, 26). These 2 approaches complement each other in characterizing growth with data-driven parameter estimates using continuous (SITAR) and categorical (LGMM) exposures. Each of these modeling approaches included an extensive evaluation of model fit for the growth curve modeling prior to estimating the association of growth characteristics and the lipid levels outcome.

Superimposition by translation and rotation. The SITAR approach (24) can extract up to 3 random effects from a nonlinear model (24, 27). First, we estimated 3 growth characteristics that indicate individual changes from the average growth curve for: 1) size (shifts up and down from the average growth curve in units used for log transformed weight (kg), length (cm), and WFL (g/cm)); 2) tempo (shifts left and right from the average growth curve relating to timing of growth in month units); and 3) velocity (a scaling factor that shrinks or enlarges the time scale from the average growth curve—larger values as parameterized according to

the model (24) indicate faster velocity). For each of the 3 anthropometric measures, we evaluated model fit for all combinations of growth characteristics and selected the set with the lowest Bayesian information criterion (BIC) as previously described for this sample (28). Weight was log transformed according to similar model fit evaluations. In a second step, we used the growth characteristics as exposure variables in separate simple linear regression models with each lipid outcome variable. For example, the velocity growth characteristic for length would be a covariate in 3 models for each of the lipid outcomes: LDL-C, HDL-C, and triglycerides.

To compare the SITAR growth characteristics with simpler methods used in prior studies, we obtained World Health Organization z scores for each of the 3 anthropometric methods, determined binary categories based on a z-score change greater than 0.67 from birthweight to month 5, and calculated the median and interquartile range of the SITAR characteristics (size, tempo, and velocity) between these 2 groups.

All nonlinear models were fitted using R (R Foundation for Statistical Computing, Vienna, Austria) (29) and the nlme package (30). To handle missing data in the SITAR models, we used the multivariate imputation by chained equations (mice) method with the mice R package (31).

Latent growth mixture models. We selected the number of weight, length, and weight-for-length classes in LGMMs after evaluating the adjusted BIC and the bootstrap likelihood ratio tests (BLRT) across quadratic and cubic models (32, 33). Any classes with fewer than 30 people were not considered. The final LGMM included a cubic polynomial model for the 6 time points from birth to 5 months. Intercept and slope growth factors were specified as random effects. We reduced the number of classes via evaluation of adjusted BIC, BLRT, and substantive meaning of trajectories upon visual examination (33). For example, following selection via adjusted BIC and BLRT, and if 2 trajectories are very close together so as to substantively denote the same type of change over time, we selected the reduced model with fewer trajectories. For the sample combining male and female participants (the pooled model), the 2-class model was the best fit for all 3 trajectories, including length, weight, and WFL trajectories. For sex-stratified analyses, fit results were similar with the exception of the male WFL 3-class solution.

To evaluate associations between growth classes and distal outcomes, we used separate models for each of the 4 lipid distal outcomes. We compared mean lipid values across the latent growth classes using the manual 3-step Bolck-Croon-Hagenaars method (34), which allows for unequal variances of distal outcomes across different groups and is robust to outliers. All LGMMs were fitted in Mplus, version 8.0 (Muthén & Muthén, Los Angeles, California) (35), with data handling in R (R Foundation for Statistical Computing) with the MplusAutomation package (36). The specified models used a full information maximum likelihood (37) in Mplus (35, 38) to handle missing data, which is valid in cases of missing-at-random data—an assumption we made with these data. Considering the multiple comparisons that occur for all the tests across 4 lipid distal outcomes, sex-stratified and pooled analyses, and 3 different types of trajectories with and without adjustment, we used a false-discovery-rate controlling procedure (39) at an alpha level of 0.05 to account for multiple hypothesis tests.

RESULTS

Of the 596 participants, the median triglyceride, LDL-C, and HDL-C (mg/dL) values at a mean age of 17 years were 73.7 (interquartile range, 56.9, 100.7), 91.7 (interquartile range, 77.6, 106.9), and 39.5 (interquartile range, 33.0, 46.4), respectively (Table 1; Web Figure 3). Approximately half (52%, $n = 311$) of the participants were male. Body size trajectories spanned 6 time points at monthly intervals with no more than 7% of observations missing at each month and no missing measurements at birth. All participants had at least 2 anthropometric observations for this time range, with an average of 6 observations per individual.

Superimposition by translation and rotation

We found a positive adjusted association between length velocity and HDL-C (mg/dL) indicating an 11.5 (95% confidence interval (CI): 3.4, 19.5)-unit increase in HDL-C (mg/dL) for a 1-unit change in the SITAR length velocity scaling factor (Figure 1; Web Figure 4; Web Table 2). Faster length growth (i.e., the velocity component) was associated with more favorable values (i.e., higher HDL-C levels). The length tempo parameter was positively associated with LDL-C (6.9, 95% CI: 1.8, 12.0) indicating that a 1-month shift in later growth timing was associated with an almost 7-mg/dL higher LDL-C. The direction of associations was similar for the same analyses for male and female participants. We did not find evidence to support an association between weight or WFL infant growth parameters and lipid values in adolescence. Higher tempo and velocity SITAR growth characteristics corresponded with the z-score thresholds denoting the simpler definition of growth acceleration (z-score change >0.67) (Web Table 3).

Latent growth mixture models

Anthropometric trajectory descriptions. After determining the maximum number of growth classes, we identified the growth trajectories with labels according to their shapes (Figure 2; Web Figure 5) and values for trajectory parameters (Web Tables 4–5): "slower," "faster," and "fastest." Upon visual inspection, weight trajectories displayed less heterogeneity compared with WFL trajectories, but they were similar to the pooled WFL trajectories in that there were 2 distinct latent growth classes: "slower" and "faster." In contrast, the length growth classes had the least heterogeneity during this time period from birth to 5 months, especially for the female group.

The sex-stratified groups for the weight and length trajectory types were similar to the pooled trajectory types with "slower" and "faster" velocity types. WFL trajectory types for the female group also had 2 types (Web Figure 5).

Table 1. Descriptive Statistics, Santiago Longitudinal Study, Chile, 1991–1996

Characteristic	Median (IQR)		
	Male (*n* = 311)	Female (*n* = 285)	Total (*n* = 596)
Triglycerides, mg/dL	71.4 (55.6, 100.1)	76.0 (58.4, 101.6)	73.7 (56.9, 100.7)
Total cholesterol, mg/dL	143.0 (130.4, 158.2)	154.0 (137.5, 169.8)	146.9 (133.0, 165.1)
LDL-C, mg/dL	89.2 (75.7, 104.3)	94.5 (80.7, 109.5)	91.7 (77.6, 106.9)
HDL-C, mg/dL	37.0 (31.3, 42.8)	42.2 (35.6, 50.3)	39.5 (33.0, 46.4)
No added iron, %[a]	158 (50.8)	125 (43.9)	283 (47.5)
Breastfeeding through month 5[a]	0.6 (0.5)	0.7 (0.5)	0.7 (0.5)
Graffar index	32.0 (27.0, 37.0)	32.0 (27.0, 37.0)	32.0 (27.0, 37.0)
Maternal age, years	26.1 (21.1, 30.8)	26.0 (21.8, 30.2)	26.0 (21.4, 30.7)
Birth weight, g	3,560.0 (3,290.0, 3,835.0)	3,450.0 (3,230.0, 3,750.0)	3,500.0 (3,260.0, 3,800.0)
Gestational age, weeks	39.0 (38.5, 40.0)	40.0 (39.0, 40.0)	40.0 (39.0, 40.0)
Adolescent body weight, kg	65.6 (58.8, 75.5)	59.5 (52.7, 68.2)	62.8 (55.8, 72.9)
Adolescent height, m	1.7 (1.7, 1.7)	1.6 (1.6, 1.6)	1.7 (1.6, 1.7)
Adolescent BMI[b]	22.3 (20.3, 25.6)	23.6 (20.7, 26.7)	22.9 (20.5, 26.1)
Adolescent age, years	16.8 (16.6, 16.9)	16.8 (16.7, 17.0)	16.8 (16.6, 17.0)

Abbreviations: BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; IQR, interquartile range; LDL-C, low-density lipoprotein cholesterol.

[a] Values are expressed as no. (%).

[b] Weight (kg)/height $(m)^2$.

In contrast to all other anthropometric measurement trajectories, the WFL trajectories for the male group had 3 types: "slower," "faster," and "fastest".

Mean lipid comparisons. Following the LGMM analyses, we found no evidence to support a strong association between infant anthropometric growth and lipid outcomes during adolescence. However, these results were largely similar in the direction of association reported for the SITAR analyses: The slower growth groups were associated with unfavorable lipid levels relative to faster growth groups (Figure 3, Web Figure 6; Web Table 6). In the pooled sample, LDL-C was higher for the "slower" vs. "faster" velocity groups for weight, WFL, and length trajectory latent class groups. For example, the "slower" weight velocity group's mean LDL-C level exceeded the "faster" weight velocity group by 5 mg/dL for both the unadjusted (6.5, 95% CI: 1.1, 11.9) and adjusted (5.3, 95% CI: −0.4, 11.0) differences (Figure 4, Web Figure 7; Web Table 7).

Of the other lipid measures considered, including HDL-C, triglycerides, and the triglyceride:HDL-C ratio, the HDL-C differences coincided with findings that unfavorable lipid levels were associated with "slower" growth groups relative to "faster" growth groups. For example, the female, male, and pooled weight trajectories indicated that the "slower" velocity groups had adjusted HDL-C that was 3.1 mg/dL (95% CI: −6.6, 0.4), 2.0 mg/dL (95% CI: −5.0, 1.1), and 1.9 mg/dL (95% CI: −4.5, 0.7) lower than the "faster" velocity group, respectively (Figure 4, Web Table 7). WFL trajectory groups also indicated similar decreases in HDL-C for the "slower" velocity group relative to the "faster" group. Differences in log(triglycerides) between growth classes were consistently close to null, as were the triglyceride:HDL ratios.

DISCUSSION

We estimated associations between growth patterns in early infancy and lipid levels in adolescence after applying 2 different methods to data collected from the Santiago Longitudinal Study, a Chilean infancy cohort followed from infancy into young adulthood. We found a positive association between the SITAR length velocity parameter and HDL-C levels in adolescence (11.54, 95% CI: 3.6, 19.5) and a positive association between length SITAR tempo parameter and LDL-C levels (6.9, 95% CI: 1.8, 12.0). We did not find evidence to support an association between different latent-class growth trajectories and lipid levels during adolescence. When examining the size of mean lipid differences across each type of trajectory, weight and WFL trajectories had the strongest associations with the LDL-C distal outcomes. In each case, the "lower" velocity group had higher LDL-C levels relative to the "high" velocity group. None of these findings support the original hypothesis of faster growth and an association with adverse lipid levels.

The positive associations between the length SITAR tempo parameter, or timing of growth, and the LDL-C levels in adolescence suggest that infants with slower growth timing have higher LDL-C levels than infants with faster timing. Slower growth timing is also associated with lower gestational age in this sample (28), suggesting that infants born

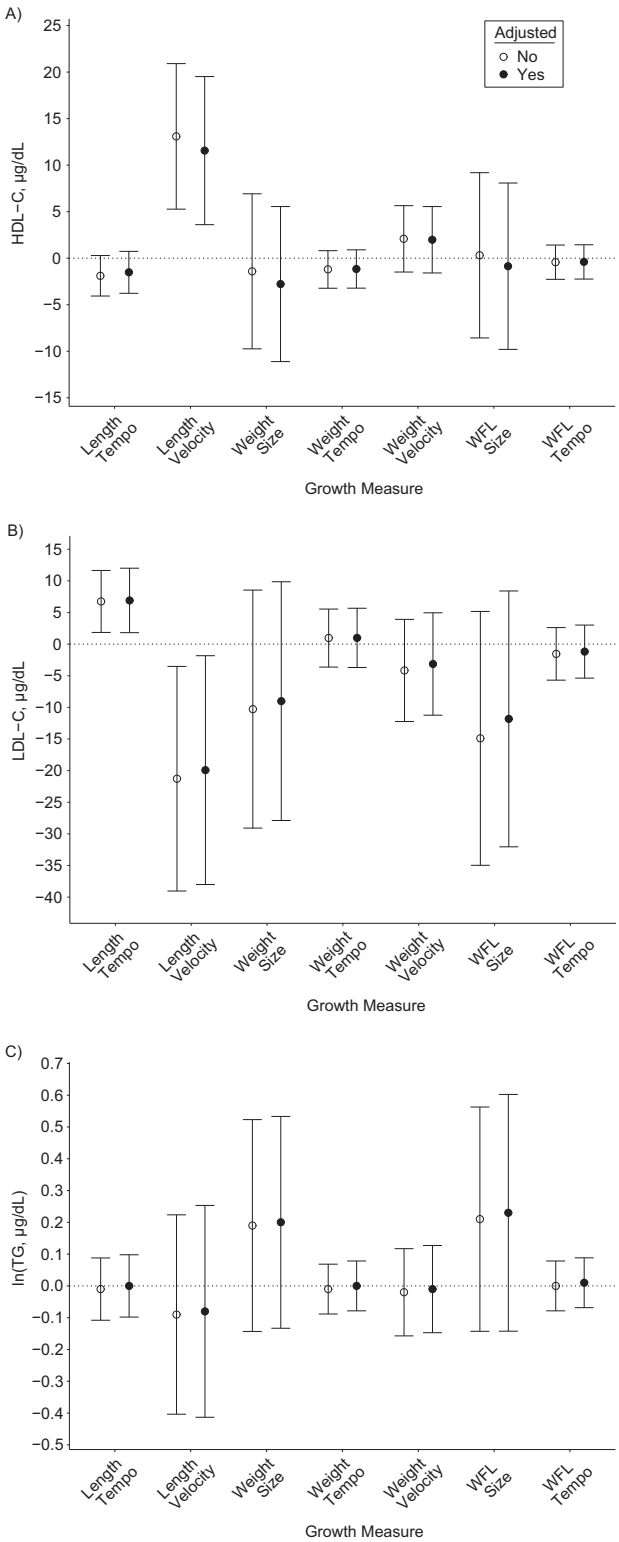

Figure 1. Coefficients for association for the pooled sample between superimposition-by-translation-and-rotation growth parameter (95% confidence interval) and lipid outcome by type of growth measure and adjustment status, Santiago Longitudinal Study, Chile, 1991–1996. A) High-density lipoprotein cholesterol (HDL-C); B) low-density lipoprotein cholesterol (LDL-C); C) natural log transform of triglyceride (TG). WFL, weight-for-length.

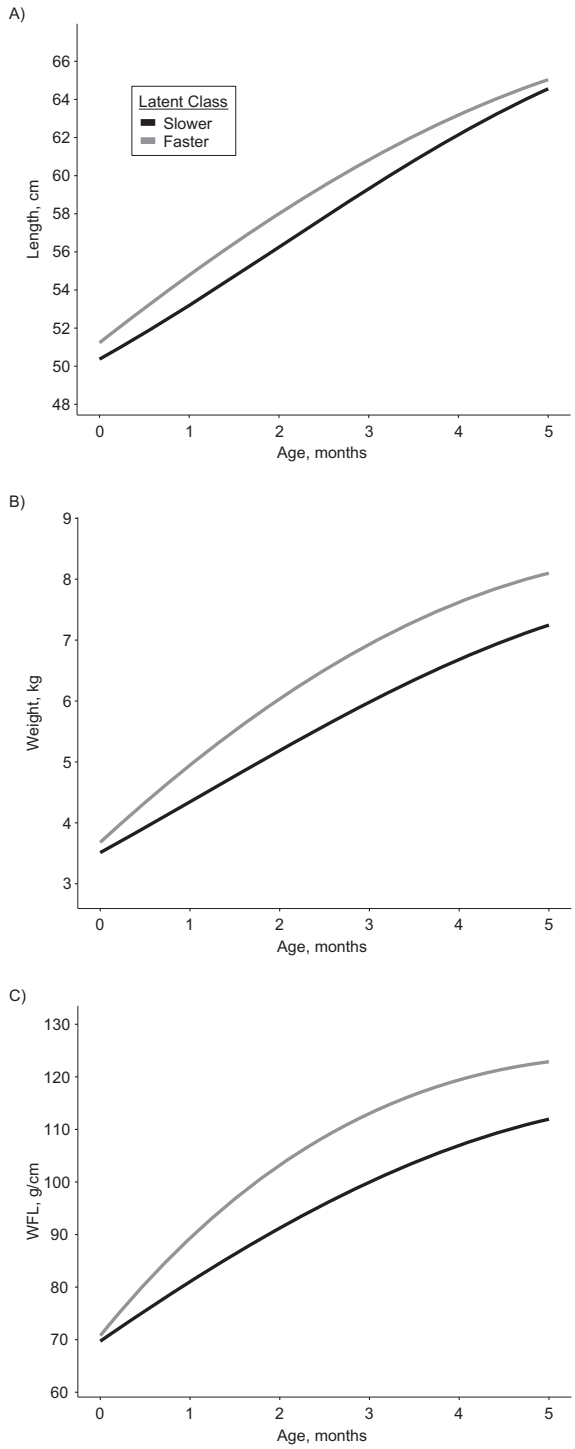

Figure 2. Growth trajectories for the pooled sample by type of trajectory and adjustment status, Santiago Longitudinal Study, Chile, 1991–1996. A) Length growth; B) weight growth; C) weight-for-length (WFL).

at earlier gestational ages may be at risk for higher LDL-C levels later in life. This type of analysis applied to infant anthropometric growth before 6 months is unique, and

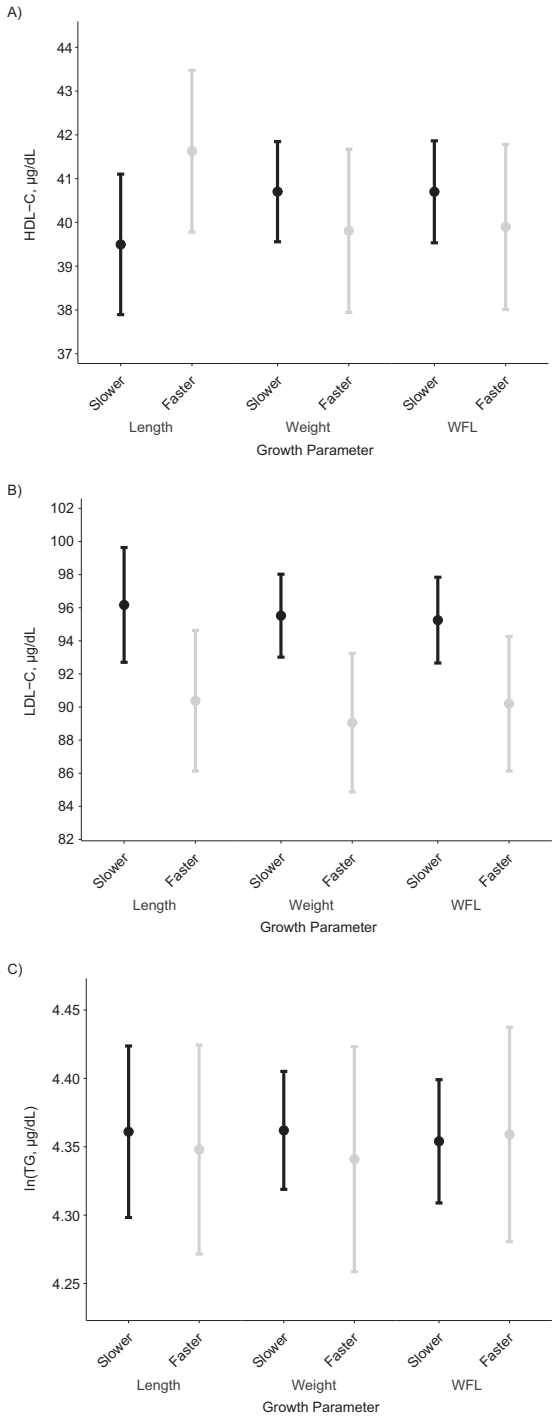

Figure 3. Mean lipid values for the pooled sample by type of distal outcome, growth parameter, and latent class, Santiago Longitudinal Study, Chile, 1991–1996. A) High-density lipoprotein cholesterol (HDL-C); B) low-density lipoprotein cholesterol (LDL-C); C) natural log transform of triglyceride (TG). WFL, weight-for-length.

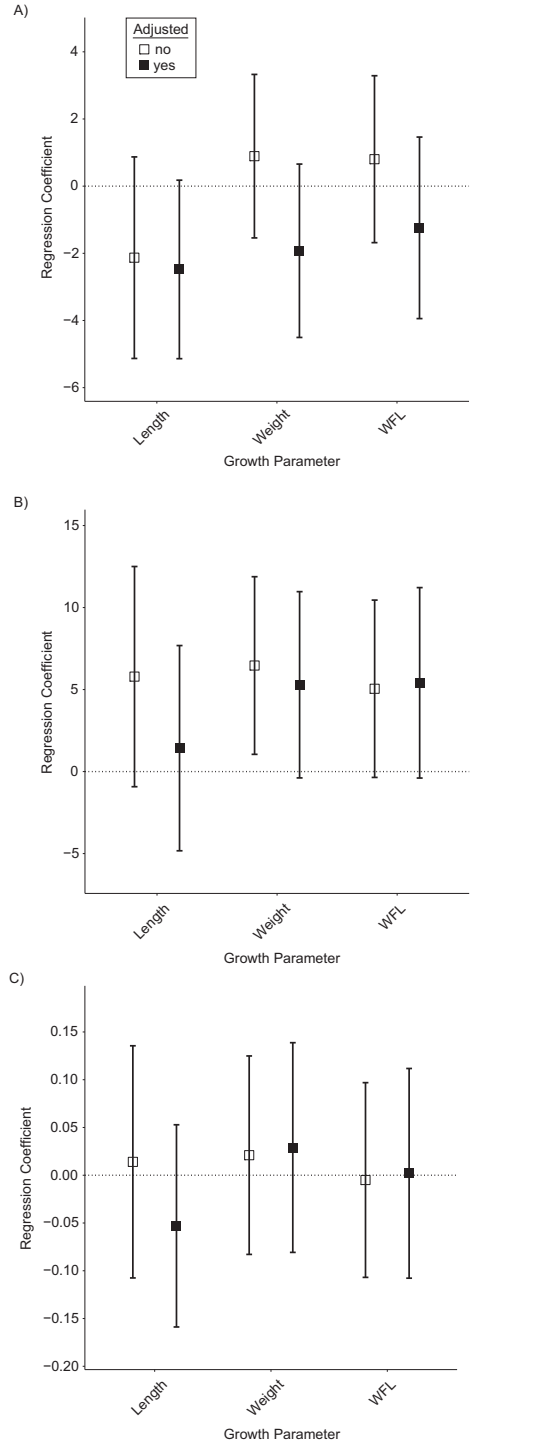

Figure 4. Pairwise growth-class differences for the pooled sample of slower vs. faster growth classes by type of distal outcome and growth parameter, Santiago Longitudinal Study, Chile, 1991–1996. A) High-density lipoprotein cholesterol; B) low-density lipoprotein cholesterol; C) natural log transform of triglyceride. WFL, weight-for-length.

replication of these findings will be necessary to confirm them.

Despite the lack of heterogeneity of length growth classes as mentioned before, the LGMM results were useful, and results from this method informed our hypothesis. When examining the associations across the 4 different lipid distal

outcome measures, LDL-C had the largest difference across all 3 types of latent growth-class trajectories, demonstrating that the "slower" growth group had the highest mean LDL-C relative to the "faster" group. This finding of the slower-growing group carrying higher risk of unfavorable lipid levels is in contrast to previous studies that have shown a positive association with rate of growth during infancy and adverse lipid levels later in life.

In terms of early infant length trajectories, faster linear (length) growth during infancy has been identified as an exposure associated with unfavorable lipid levels later in life (7–10). In contrast to these prior findings, the length velocity parameter from the SITAR model, indicating how fast an infant grows, was positively associated with HDL-C levels, considered a protective factor for cardiovascular disease risk. Most studies of growth during infancy focus on weight or some combination of weight and length, including weight-for-length, body mass index (weight (kg)/height $(m)^2$), or the ponderal index (kg/m). Studies with length-change measures including growth after the first 6 months of infancy (8, 12) indicate no evidence for an association with lipids, but the direction of associations are in line with unfavorable associations with faster growth. For example, studies of lipid levels in children at an average age of 4 years (8) and an age range including the first 2 years of life (12) suggest an adverse association between length change and lipids. The difference in ages at outcome and different growth time ranges across these studies may account for contrasts with our results that demonstrate a positive association between length growth characteristics in early infancy as an exposure and an outcome of favorable lipid levels more than a decade later.

There is some previous evidence of a positive association between peak length velocity and HDL-C (12) after adjusting for a mediating factor, body mass index during adulthood. This positive association between faster growth and a favorable lipid profile is similar to the results from our analyses despite differences across populations, cohort timing, and type of measure. Also, this data from a European cohort was collected around 3 decades prior to the SLS, and it included peak weight velocity, a different measure from the average velocity measure in this study. However, similar to the approach in this paper, this study used a parametric form of growth accompanied by multiple early measures of weight and length. The similarity between the 2 studies suggests we can obtain more nuanced information regarding associations between growth and outcomes based on a richer set of anthropometric measures over time.

Methodological differences between this study and previous studies make it difficult to explain the differences in the direction of association when examining WFL growth trajectories. Some factors that can account for these differences include secular time effects, varying endpoint ages, different populations, different statistical methods, or a combination of all of these. For example, another Chilean study, less than a decade after SLS (8) indicated weight change having a positive association with adverse lipid levels for those with exclusive or predominant breastfeeding. In that study, the endpoint age, 5 years, was around 12 years less than the outcome age in our analyses, and growth change was assessed with methods suitable for 2 observations over time, both of which could explain the differing results. Another more recent study in a group of Canadian children (40) indicated a positive association between growth in the first 2 years of life and unfavorable HDL-C levels. There were 3 or more observations in the infant growth period, and this period spanned the first 2 years—a wider age span than what we used to measure trajectories. Growth in the first 5 months of life may function as a different exposure than the broader span of age in the Canadian study, and this explanation may account for the differing associations between the 2 studies.

These examples underscore the need to separate out time periods when assessing associations between infant growth and cardiometabolic outcomes, the first 6 months in particular. Other studies looking at coronary heart disease outcomes in adults, considered farther downstream than the examined exposure of lipid levels measured in adolescence, also are associated with slower growth before 1 year and support examining growth during this time (41, 42). Our findings include higher-length-velocity and lower-tempo growth characteristics associated with favorable lipid profiles, suggesting that an infant in the first 6 months who begins the growth process earlier and grows faster may have higher HDL-C and lower LDL-C values later in life relative to infants with average growth measures in the sample. Furthermore, these differences may have consequences for interventions targeting different age groups designed to lower cardiometabolic risk factors. For example, pending further evidence supporting the positive association between length velocity and a favorable lipid profile, modifiable pathways and public health interventions may include efforts to improve nutrition and standard of living conditions associated with infant length and adult height status (43).

Limitations

Some limitations of this study included the small sample size and factors relating to causal effect estimation. This sample size of less than 600 individuals is small for LGMM analysis (44), and it can preclude detection of smaller, but important, growth patterns. In addition to sample size, the conceptual issue of using growth as an exposure limits inference regarding any underlying biological mechanism. Growth is a proxy for different biological mechanisms, including types of feeding, such as a higher-fat diet, or lower amounts of food, such as those used in experimental animal studies to alter early postnatal growth. Assessing growth limits an explanation of the biological mechanism by which the association may occur. However, the growth variables may have much less measurement error than the factors underlying them, for example, diet and fat consumption.

Issues with the sample included the lack of low birth weight (LBW) and/or preterm infants, which may partly explain the differences we noted above with other studies that may include this group. However, LBW infants and preterm births are a small proportion of births, usually less than 10% (45), and we do not expect this omission to substantively alter coefficients estimating the association between growth and lipid levels. Furthermore, the SITAR method

uses deviations from the average growth characteristics, and we would expect LBW infants to have more extreme growth values relative to the mean, contributing to larger differences. If following similar patterns from these results, we would expect our estimates to be attenuated compared with a sample with LBW and/or preterm births and more extreme growth measures. Also, our results may not generalize to other groups, given the source of our analytical sample from low- to middle-income, working-class, neighborhoods in Santiago, Chile. Last, our estimates do not distinguish between indirect and direct estimates of the association between early infant growth and lipid outcomes during adolescence. Future study of the potential for indirect effects, including child growth during age intervals up to our adolescent endpoint that function as mediating factors, may help explain the association between faster early growth and favorable lipid levels.

Strengths

Strengths of this study included the specification of a well-characterized and comprehensive array of anthropometric observations (weight, length, and WFL) in infancy and lipid measurements (HDL-C, LDL-C, triglycerides, and HDL-C: triglyceride ratio) in the same individuals during adolescence, and 2 distinct analytical approaches in understudied populations: low- to middle-income Hispanic/Latinos. The combination of exposures and outcomes allowed comparisons as to which distal lipid outcome had the strongest effect within particular types of trajectories. By leveraging the large number of repeated observations before age 6 months, we were able to obtain a more nuanced picture of growth that is not fully captured by binary thresholds based on fewer observations, such as a *z*-score change across 2 time points of >0.67. Our strongest associations were observed between LDL-C and weight and WFL trajectories. In designing future analyses, it may be worth designating LDL-C as the primary outcome to maximize power. Another advantage was the side-by-side use of the 2 distinct analytical techniques of SITAR and LGMM, which allowed comparisons of analytical approaches. The SITAR method was more informative than the LGMM method in assessing length trajectories in this early period of life before 6 months of age, given the lack of heterogeneity of growth patterns.

Conclusion

We found an association between faster growth patterns before 6 months and favorable lipid levels in adolescence after applying 2 different methods with data collected from the Santiago Longitudinal Study, a Chilean infancy cohort followed from infancy into young adulthood. Our data did not support our hypothesis of an association between faster growth before age 6 months and adverse lipid level in adolescence. Our assessment of a wide array of exposure and lipid outcome measures, representing a comprehensive analysis of growth patterns in this particular age period, is unique in the literature. Replication of these findings with similar time periods and methods in other populations could provide evidence of generalizability outside of this Chilean cohort. Our findings also emphasize the importance of more studies that collect repeated anthropometric measures during early infancy and lipid levels in adolescence to gain a better understanding of the relationship between infant growth and a favorable lipid profile in adolescence and adulthood.

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