Effects of Acute Diarrhea on Linear Growth in Peruvian Children

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Linear growth retardation during childhood is a determinant of short stature and impaired capacities in adults of developing countries. To study the effect of diarrhea on height during childhood, the authors followed a birth cohort of 224 Peruvian children for 35 months with records of daily diarrhea and monthly anthropometry. This study was conducted from April 1995 to December 1998. At 24 months of age, study children were 2.5 cm shorter than the US National Center for Health Statistics/World Health Organization growth reference. A diarrheal prevalence of 2.3% in the first 24 months of life explained 2–27% of this growth deficit. There was a 2-month delay before the effects of diarrhea on height became manifest. Height deficits were proportional to diarrheal prevalence. For example, children ill with diarrhea 10% of the time during the first 24 months were 1.5 cm shorter than children who never had diarrhea. In addition, the adverse effects of diarrhea on height varied by age. Diarrhea during the first 6 months of life resulted in long-term height deficits that were likely to be permanent. In contrast, diarrhea after 6 months of age showed transient effects. Study results indicate that diarrhea control, especially during the first 6 months of life, is likely to improve linear growth in Peruvian children.

Linear growth (height) retardation during early childhood is highly prevalent in developing countries (1) and contributes to short stature and impaired capacities in adults (2). Short stature is disproportionately prevalent among the poor. Indeed, previous studies have documented that in developing countries, underprivileged children grow substantially less than do children in high socioeconomic strata or children in more developed countries (1). Height deficits in children from the developing world are more strongly related to poverty and other environmental influences than to genetic influences in body size, despite differences in ethnicity across socioeconomic strata (1). In light of this evidence, the World Health Organization (Geneva, Switzerland) recommended the US National Center for Health Statistics (Hyattsville, Maryland) (NCHS/WHO) growth curves as the international growth reference (3). Environmental factors, such as inadequate nutrition (4), lack of safe water and sanitation (5), and high prevalence of infections, are common among the poor and may affect the normal growth of children (6).

The relation between infection and nutrition, and in particular the effect of diarrheal diseases on childhood growth (6–8), has been intensively investigated. The short-term effects of diarrhea on growth have been well documented. In fact, seminal work nearly 30 years ago in Santa María Cauqué, Guatemala, suggested that diarrhea was a determinant of poor weight gain in children (9). Subsequent community-based cohort studies in different geographic and social settings have documented adverse effects of diarrhea on childhood growth, in terms of both weight and height (10–14). However, the finding that recurrent episodes of acute diarrhea lead to permanent growth retardation has been challenged by several reports suggesting that children recover (catch up) from their early deficits (15–17). For example, Briend et al. have claimed that in Bangladesh, the effect of

Abbreviations: AED, attributable effect of diarrhea; CAR(1), first-order continuous autoregressive; CI, confidence interval; NCHS/WHO, National Center for Health Statistics/World Health Organization.

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diarrhea on growth was transient and that children experienced complete catch-up growth even after repeated episodes of acute diarrhea (15).

Studies of the effects of diarrhea on growth that use short time intervals may overestimate growth deficits because short intervals do not allow time to detect possible catch-up growth. On the other hand, they may underestimate growth deficits because they do not allow time to detect possible delayed effects. Thus, our specific aim for this study was to answer the following questions: 1) Did diarrhea have an immediate or a delayed effect on linear growth; if so, 2) was it transient or permanent? A secondary aim was to study the relation between childhood height and maternal stature.

MATERIALS AND METHODS

We conducted a cohort study between April 1995 and December 1998 to determine the relation between height and diarrhea in 224 children from Pampas de San Juan, a peri-urban community in Lima, Peru. Data collection has been described elsewhere (18). Briefly, children were recruited at birth between April 1995 and April 1998 and were followed for 35 months. Demographics were collected at recruitment.

Outcome

Height was recorded monthly to the nearest 0.1 cm. Recumbent length was measured by using a locally made length platform and sliding footboard for children younger than age 2 years. Standing height was measured by using a locally made platform and movable headboard for children aged 2 years or older. We compared the height measurements in our study with the NCHS/WHO international reference (3).

Predictors

Predictors for height included age, history of diarrhea since birth, gender, breastfeeding, water supply, sanitation, water storage, and maternal stature. We classified breastfeeding status into three categories: none, mixed, and exclusive breastfeeding. We classified water supply as home connection (+1), cistern truck or community standpipe (+2), and water obtained or purchased from a neighbor (+3). If water was stored in the household, we classified the container size as large (+1), medium (+2), and small (+3). Water storage quality was measured by using the size of the smallest container in the household. Sanitation facility was classified as sewage connection (+1), latrine or equivalent (+2), and no facility available (+3). (Scores assigned to each category are given in parentheses.) We calculated a summary score for water supply, sanitation, and water storage as the sum of the scores assigned for each of the three variables. Maternal stature was measured with an adult-size footboard and metric rule.

History of diarrhea

Diarrheal surveillance was conducted daily. At each daily visit, field workers asked the mother or caretaker if the child was ill with diarrhea and, if so, about the number of liquid or semiliquid stools the child had passed during the day of the visit. An episode of diarrhea started with the first day on which the mother indicated that her child had diarrhea and ended on the last day of diarrhea after which the child passed fewer than three liquid or semiliquid stools in each one of two consecutive days. A day of diarrhea was defined as any day during the duration of an episode. A persistent episode of diarrhea lasted 14 days or longer (19).

We defined period prevalence of diarrhea in the first t months of life as the number of days on which diarrhea was recorded from birth to t months of age divided by the total number of child-days observed during that period.

Both incidence and duration of diarrhea may affect height. Thus, we examined their combined effects with regression models that related height to the number of days with diarrhea. The period prevalence of diarrhea was the series of days that the child had diarrhea in each of his or her monthly intervals. To build the history of diarrhea for each child, we identified a series of consecutive 31-day (monthly) intervals that spanned the child’s follow-up period (figure 1). For each monthly interval, we counted the days with diarrhea in that interval (figure 2). The number of days with diarrhea can be interpreted as a diarrheal prevalence because every monthly interval contains the same number of follow-up days.

The model expressed height measured at age t months in terms of the history of diarrhea between birth and age t months. Diarrheal surveillance was 94 percent complete; fewer than 1 percent of censored intervals were longer than 1 month. Since both the prevalence of diarrhea and the proportion of censored intervals were small, we considered censored intervals as if they were diarrhea free. The lag order (k) indexed the monthly intervals. For t months of age, the kth lagged interval was the time period between ages (t − k) and (t − k + 1) months. The purpose of the lags was to measure the delayed effects of diarrhea on linear growth. We estimated the effects of diarrhea on height by using 32 lags. We did not have enough data to estimate the effects of lags larger than k = 32.

Biostatistical methods

To examine the effects of diarrhea on height, we used general linear mixed models (20). Random effects modeled growth heterogeneity in height among children (21). A first-order continuous autoregressive or CAR(1) error term modeled the serial correlation among measurements within the same child (22).

Our analysis proceeded in two steps. First, we developed a growth model using our height data; second, we included the age-specific effects of diarrhea on height in our growth model. We used regression splines to model both growth curves and age-specific effects of diarrhea on height. Although height measurements for each child were scheduled at regular monthly visits, they were not always obtained exactly a month apart or were not obtained for all scheduled visits. Regression splines enabled us to analyze longitudinal growth data meas-
ured at irregular intervals and provided smooth age-specific estimates that could be interpreted graphically.

**Step 1.** The dependent variable in our growth model was height. We included new covariates in the growth model in a stepwise manner. In each step, we assessed the regression fit via a likelihood ratio test, and we conducted model diagnostics. The first covariate in the model was age. We expressed age as a linear combination of regression spline elements. The number of regression spline elements depended on the number of internal knots (23). Our analysis used natural cubic splines. A natural cubic spline with $p$ internal knots uses $p + 2$ elements; however, only $p + 1$ elements are required if the regression model includes an intercept (24). We used equally spaced age quantiles for the internal knots. We increased the number of internal knots until the decrease in $-2 \log$ maximum likelihood was not significant at the $\alpha = 0.05$ level. We evaluated the statistical significance of the random effects and CAR(1) terms. The best diagnostic results were obtained when a random intercept and random effects for age and the logarithm of age were included in the regression model. The growth model consisted of a regression spline with six internal knots, a random intercept, random effects for age and the logarithm of age, and a CAR(1) error term.

**Step 2.** To incorporate diarrhea into the model, we regressed height on the history of diarrhea available from the child’s birth to the time of the height measurement. We included the history of diarrhea in the model as the number of days on which diarrhea occurred for each monthly interval. We modeled age-specific coefficients of each lagged exposure to diarrhea with a regression spline, and we

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**FIGURE 1.** Lagged days of diarrhea per monthly interval. Each circle on the height growth curve of a child in the study cohort represents a height measurement. For each anthropometric measurement, consecutive monthly intervals were constructed spanning the follow-up period. Horizontal segments represent these consecutive monthly intervals. For each monthly interval, the number of days on which diarrhea occurred (prevalence) entered the analyses; this number can be interpreted as a diarrheal prevalence because every monthly interval contains the same number of follow-up days.

**FIGURE 2.** Lagged days of diarrhea per monthly interval for a child between ages $t - 8$ and $t$ months. Eight lagged periods were constructed for one anthropometric measurement.
modeled each coefficient with a separate regression spline. We included an indicator to account for any disjunction between recumbent length and standing height, and we controlled for the potentially confounding effects of breastfeeding practices, water supply, sanitation, water storage, gender, and maternal height.

Regression model

The regression model was as follows:

\[ y_{ij} = \alpha + U_i + \sum_{r=1}^{p+1} \beta_r N_r(t_{ij}) + \sum_{k=1}^{32} \gamma_k(t_{ij})d_{ik}(t_{ij}) + \delta I(t_{ij} \geq 24) + \sum_{m=1}^{6} \tau_m c_{jm}(t_{ij}) + \epsilon_{ij}, \]

where \( i (= 1,\ldots,n) \) indexed the children in the sample; \( j (= 1,\ldots,n_i) \) indexed the height measurements of child \( i \); \( y_{ij} \) was the \( j \)th height measurement for child \( i \); \( t_{ij} \) was the age at which the height was observed; \( \alpha \) was the intercept; \( U_i, t_{ij} \) were \( (U_i, t_{ij}, s) = (\alpha_i + \beta_1 t_{ij} + \phi_\log(t_{ij} + 1)) \) was the random effect of child \( i \) and \( s \) indexed gender (\( s = 0 \) for males and \( s = 1 \) for females); and

\[ \sum_{r=1}^{p+1} \beta_r N_r(t) \]

was a regression spline that modeled the expected height curve for a child who never had diarrhea. The \( N_r(t) \) were the spline elements and \( (\beta_1,\ldots,\beta_{p+1}) \) were the regression parameters; \( p \) was the number of internal knots for this regression spline; for child \( i, d_{ik}(t) \) was the number of days on which diarrhea occurred between ages \((t - k)\) and \((t - k + 1)\) months and \( \gamma_k(t) \) was its associated coefficient; \( I(t_{ij} \geq 24) \) was the indicator with value 0 if \( t < 24 \) months of age and 1 otherwise, and \( \delta \) was its associated regression parameter; \( c_{ij}(t),\ldots,c_{6i}(t) \) were the confounding variables for child \( i \) and \( \tau = (\tau_1,\ldots,\tau_6) \) were regression parameters; and \( \epsilon_{ij} \) were CAR(1) random errors (22).

We controlled for the effect of the following confounders: breastfeeding (exclusive or mixed); quality of the water supply, sanitation, and water storage; gender of the child; and mother’s height. We included breastfeeding in the model with two time-dependent indicators, one for exclusive breastfeeding (\( c_{3i}(t) = 1 \) if the child \( i \) was exclusively breastfeeding at time \( t \), \( c_{3i}(t) = 0 \) otherwise) and the other for mixed breastfeeding (\( c_{4i}(t) = 1 \) if the child \( i \) was breastfeeding but eating or drinking other foods at time \( t \), \( c_{4i}(t) = 0 \) otherwise).

We included the quality of the water supply, sanitation, and water storage in the model with an ordinal score (\( c_{3i} = 3,\ldots,9 \), with low values indicating better levels). We included gender with an indicator (\( c_{5i} = 0 \) if male, \( c_{5i} = 1 \) if female) and maternal stature as the difference (\( c_{5i} = h_i - \bar{h} \)) between the mother’s height for child \( i \) (\( h_i \)) and the sample average (\( \bar{h} \)). We included an interaction term between child’s age and maternal height (\( c_{6i} = (h - \bar{h}) \times t \)).

The age-specific coefficient \( \gamma_k(t) \) associated with the \( k \)th-lagged interval \( d_{ik}(t) \) measured the height difference per day of diarrhea between children who were \( t \) months of age and who had diarrhea between \((t - k)\) and \((t - k + 1)\) months of age and children of the same age who did not have diarrhea. The \( \gamma_k(t) \) were modeled with regression spline functions, namely,

\[ \gamma_k(t_{ij}) = \sum_{v=1}^{q_k+1} \lambda_{kv} M_{kv}(t_{ij}), \]

where \( k (= 1,\ldots,32) \), indexed the lag; \( M_{kv}(t_{ij}) \) were spline elements, and \( \{\lambda_{kv}, \nu = 1,\ldots,q_k + 1\} \) were the regression parameters for regression spline \( \gamma_k(t) \) with \( q_k \) internal knots equally spaced between \( k \) and \( \max(t_{ij}) \). The number of internal knots \( q_k \) for \( \gamma_k(t) \) decreased with increasing values of \( k \) and ranged from one to four. The boundary condition specified that the value of the spline was zero at \( t = (k - 1) \).

We estimated the height deficit at \( t \) months of age associated with the history of diarrhea (the attributable effect of diarrhea, or AED) by using the following equation:

\[ \operatorname{AED}(t) = \frac{1}{n_i} \sum_{j=1}^{n_i} \sum_{k=1}^{t} \hat{\gamma}_k(t) d_{ik}(t), \]

where \( n_i \) was the number of children followed through \( t \) months of age, \( \hat{\gamma}_k(t) \) indexed these children, \( d_{ik}(t) \) was described above, and \( \hat{\gamma}_k(t) \) estimated \( \gamma_k(t) \). We generated 2,000 bootstrap estimates and used the 2.5 and 97.5 percentiles to form 95 percent bootstrap confidence limits for \( \operatorname{AED}(t) \) (25).

For our analyses, we used SAS version 7 software (SAS Institute, Inc., Cary, North Carolina), and S-Plus 2000 software (MathSoft, Seattle, Washington).

RESULTS

For 230 children recruited at birth, anthropometric data and diarrheal histories were complete; however, maternal height was missing for six children whose data were not entered in the analysis. For the remaining 224 children, there were 5,038 height measurements. The number of height measurements varied by child from six to 37, and the average time between field visits was 33 days.

Descriptive statistics for child height

The study children were shorter than the NCHS/WHO growth reference. During the first months of their lives, the deficit was small. At 3 months of age, boys had a mean deficit of 0.5 cm and girls a deficit of 0.2 cm relative to the NCHS/WHO reference. By 24 months of age, boys had a mean height deficit of 2.6 cm and girls a deficit of 2.4 cm. For the purpose of comparability with other studies, this paper reports results on the effects of diarrhea on height at 24 months of age. Although our model estimated that boys were taller than girls at birth by 1.3 cm (\( p < 0.001; \) Wald test), their growth velocities were not significantly different (\( p = 0.11; \) likelihood ratio test). Our model estimated a disjunction between recumbent length and standing height of 0.1 cm; however, this difference was not significant at the 0.05 level.

Descriptive statistics for diarrhea

The 224 children experienced 3,335 days of diarrhea during 156,436 observed child-days. These children had
1,359 diarrheal episodes and were ill with diarrhea 2.1 percent of the time. The mean diarrheal incidence was 3.2 episodes per child-year, and the number of episodes among children ranged from one to 31 during their follow-up time. Eleven percent (25/224) of the study children never had diarrhea. Among those who had diarrhea, the period prevalence ranged from 0.1 percent to 21 percent of the follow-up time. Most diarrheal episodes were of short duration, and fewer than 2 percent of the episodes lasted 14 days or longer. Diarrhea varied by age (figure 3). A greater diarrheal occurrence than 2 percent of the episodes lasted 14 days or longer. Diarrhoeal episodes per child-year, and the number of episodes among children ranged from one to 31 during their follow-up time. Eleven percent (25/224) of the study children never had diarrhea. Among those who had diarrhea, the period prevalence ranged from 0.1 percent to 21 percent of the follow-up time. Most diarrheal episodes were of short duration, and fewer than 2 percent of the episodes lasted 14 days or longer. Diarrheal prevalence varied by age (figure 3). A greater diarrheal prevalence was associated with shorter stature (table 1).

**Effects of diarrhea on child height**

The adverse effects of diarrhea on height did not manifest acutely (figure 4); rather, there was at least a 2-month delay. Diarrhea that occurred 1 month prior to the height measurement \((k = 1)\) did not significantly affect linear growth regardless of age. On the other hand, diarrhea that occurred 2–4 months prior to the height measurement \((k = 2,3,4)\) had significant adverse effects on linear growth.

The long-term effects of diarrhea on height depended on the age at which the illness occurred. Figure 5 displays a significant decline in linear growth in each age panel associated with diarrhea during the first 6 months of life and with diarrhea lagged 2–6 months prior to the age at which height was measured. Children with a history of diarrhea before 6 months of age had a period of slower growth in height followed by retarded growth not recovered later in their follow-up. These unrecovered height deficits remained present even after we controlled for diarrhea at later ages. In contrast, diarrhea that occurred after 6 months of age was associated with a transient height deficit followed by a period of partial to full catch-up growth. For example, a child aged 24 months who had diarrhea for 5 percent or more of the time in the first 6 months of life was 0.7 cm shorter (95 percent bootstrap confidence interval (CI): 0.1 cm, 1.3 cm) than a child of equal age who did not have diarrhea during that same period. Similarly, a child aged 24 months who had diarrhea for 5 percent or more of the time in the 2–6 months prior to the height measurement was 0.5 cm shorter (95 percent bootstrap CI: 0.1 cm, 0.8 cm) than a child of equal age who did not have diarrhea during that period. Six months later, at age 30 months, the height deficit associated with a diarrheal prevalence of 5 percent or more during the first 6 months of life remained at 0.8 cm, while the deficit associated with a diarrheal prevalence of 5 percent or more between ages 18 and 23 months decreased to ~0.7 mm.

The adverse effects of diarrhea on linear growth were increasingly severe in children with a greater prevalence of disease (figure 6). The average period prevalence of diarrhea in the first 24 months of life was 2.3 percent, and the mean height deficit for children in our study relative to the NCHS/WHO reference was 2.5 cm. At 24 months of age, this mean prevalence was associated with a mean height deficit of 0.4 cm (95 percent bootstrap CI: 0.1 cm, 0.7 cm) relative to children who never had diarrhea, and it explained 16 percent (2–27 percent) of the height retardation in our study sample. When the period prevalence in the first 24 months of life was 6 percent, the height deficit was 0.8 cm (95 percent bootstrap CI: 0.1 cm, 1.3 cm); when the period prevalence was 10 percent, the height deficit was 1.5 cm (95 percent bootstrap CI: 0.3 cm, 2.4 cm).

**Effects of maternal stature on child height**

Children of taller mothers were taller than their peers. In our study sample, average maternal stature was 149.4 cm. From our model, we estimated that at \(t\) months of age, children were \(0.6 + 0.04 \times t\) mm taller \((p < 0.001; \text{Wald test})\) per centimeter increase in maternal stature. At 24 months of age, there was a 1.5-mm increase in childhood linear growth per centimeter increase in maternal height. Therefore, a 10-cm difference in maternal stature corresponded to a 1.5-cm (95 percent CI: 0.8 cm, 2.2 cm) height deficit for a child aged 24 months.

**DISCUSSION**

Linear growth retardation was highly prevalent among underprivileged Peruvian children. In our study, the average child aged 24 months was 2.5 cm shorter than the international height reference. Diarrhea was a significant determinant of the height deficit during childhood. A period diarrheal prevalence of 2.3 percent (average prevalence) in the first 2 years of life was associated with 2–27 percent of the observed height retardation. Both the history of diarrhea since birth and the earliest age at which the child became ill with diarrhea contributed to explaining the effect of diarrhea on height. That is, children who had a history of diarrhea during their first 6 months of life

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had significant height deficits that were not recovered later in their follow-up. Those who had a history of diarrhea after 6 months of age, however, had height deficits after diarrhea that were partially to fully recovered later in their follow-up.

Our analysis revealed two important connections between diarrhea and height in children. First, the effect of diarrhea on height was delayed by at least 2 months. Studies that do not account for the interaction between age and diarrhea are likely to underestimate the effects of diarrhea on height. Second, diarrhea during the first 6 months of life was associated with permanent growth deficits, while diarrhea at later ages had transient effects on height. Studies that do not account for this interaction are likely to underestimate the effects of diarrhea on height. Briend et al. in Bangladesh (15) did not find long-term effects of diarrhea on height; however, their data were limited to children older than age 6 months.

In our study, diarrhea during the first 6 months of life was an important predictor of long-term stunting. In developing countries, where environmental sanitation is poor and energy intake is generally inadequate, stunted infants are not likely to catch up in height later in childhood or adolescence (1). A study in Guatemala documented that height at 3 years of age was strongly correlated with final adult height (26). Evidence from several studies has suggested that growth during infancy and childhood is critical for optimal growth during adolescence and is a significant determinant of final adult size (27). Small adult size resulting from a failure to reach full growth potential has been linked to impaired mental development (28), reduced work capacity (29), and next-generation effects on birth weight (30) and stature (26).

We also found that the association between diarrheal prevalence during the first 6 months of life and subsequent height deficits remained statistically significant even after controlling for diarrheal episodes at later ages. This study agrees with our previous finding that children less than 6 months of age who become infected with Cryptosporidium parvum do

FIGURE 3. Prevalence of diarrhea in Peruvian children aged 0–35 months, 1995–1998. The point prevalence of disease at $t$ months of age was the ratio between the number of days in which diarrhea occurred and the total number of child-days observed at each exact age in months. Top panel, point prevalence of diarrhea, defined at age $t$ months as the number of days in which diarrhea occurred divided by the number of child-days observed between $t ≤ x < t + 1$ months of age; bottom panel, period prevalence of diarrhea, defined in the first $t$ months of life as the number of days in which diarrhea occurred recorded from birth to $t$ months of age divided by the total number of child-days observed in that period. Height of each bar in this panel, period prevalence.
not recover height deficits associated with the infection, while those who become infected with \textit{C. parvum} later in life experience a period of slower growth followed by a period of catch-up growth (31). This report shows that diarrhea after 6 months of age had a transient effects on linear growth, that is, the associated height deficit was subsequently recovered. Children less than 6 months of age grow at a faster rate than do older children but have less developed digestive and immune systems (32, 33). They have not had time to develop a mature intestinal flora (34), making them more susceptible to colonization by enteric pathogens. Young infants may also sustain more severe intestinal damage than older children because of their immunologic deficiencies, impairing their ability to absorb nutrients. Nutrient losses are likely to have more severe effects in infants because they grow faster than older children. Younger children may also take longer than older children to recover from the pathophysiologic effects of diarrheal pathogens.

The results of this study and of our previously published work (18) point toward a bidirectional relation between achieved physical stature and diarrhea. A greater prevalence of diarrhea was associated with shorter stature. Conversely, a decrease in height for age was associated with a greater risk of diarrhea. While it may appear that a height deficit is both a

\textbf{FIGURE 4.} Effects of lagged days of diarrhea on linear growth in Peruvian children, 1995–1998. Each panel represents the effect of diarrhea on height at the time of diarrheal illness. The x-axis represents the age of the child at which height was measured; for example, the top panel shows the effects of the 1-month lagged days of diarrhea by age. Zero-level broken horizontal lines represent the null hypothesis of no growth difference between children ill with diarrhea and children who never had diarrhea, the filled boxes represent the effect of 1 day of diarrhea on height, a negative value represents linear growth retardation, and the vertical segments are 95% confidence intervals.
cause and a consequence of diarrhea, the results of these studies need to be interpreted in the context of the data used in our analyses. Diarrhea is an objective measure of disease in children, and its direct effect on height can be easily estimated with a statistical model. On the other hand, height for age is a nutritional indicator that represents the combination of multiple factors such as diet, genetics, and infectious processes. The multifactorial quality of this indicator complicates interpretation of the association between malnutrition and diarrhea. Nonetheless, the value of height for age as a predictor of disease risk cannot be overlooked given that this nutritional indicator can be obtained easily.

Whether a nutritional deficiency or diarrhea is first responsible for development of the vicious cycle between malnutrition and infection still remains a topic of controversy. We have not been able to find a study that has examined this point. With our data and state-space bivariate models for malnutrition and infection, one can study the joint dynamics of these two outcomes. Although such a rigorous analysis goes beyond the scope of this article, our statistical model enabled us to establish that diarrhea during the first 6 months of life resulted in linear growth decelerations that were measurable later in childhood. Furthermore, our analytical approach accounted for complex age-specific patterns of diarrheal prevalence on height not examined previously (10–

FIGURE 5. Effects of history of diarrhea on linear growth in Peruvian children aged 0–35 months, 1995–1998. Each panel represents the effect of the lagged days of diarrhea on height at a particular age; for example, the top panel shows the effects of the history of diarrhea on height at 21 months of age. The x-axis represents the age of the child at the time of diarrheal illness. Zero-level broken horizontal lines represent the null hypothesis of no growth difference between children ill with diarrhea and children who never had diarrhea, the filled boxes represent the effect of 1 day of diarrhea on height, a negative value represents linear growth retardation, and the vertical segments are 95% confidence intervals.
These results further suggest that diarrhea plays a fundamental role in early development of the vicious cycle between malnutrition and diarrhea.

Other strengths of this study include the large quantity of data collected from the children and the high level of completeness of daily diarrheal surveillance. Our study design could be improved by measuring energy, protein, or micronutrient intakes. For example, micronutrients such as zinc are known to benefit nutritional status (35). Nutritional intakes are also important determinants of linear growth (4), and their overall effects on height are likely to depend on the interaction with the effects of diarrhea on height (36). Although we collected data on the severity and etiology of diarrhea, we did not account for these disease determinants in this report. An earlier study by Black et al. reported that diarrhea caused by *Shigella* was associated with significant adverse effects on linear growth (10), which warrants further analysis of our data by etiology.

Maternal stature was an important predictor of childhood height. Our finding is similar to that of earlier studies (11, 37, 38). In an earlier study in Peru, Frisancho et al. noted that maternal nutritional status during pregnancy had profound effects on prenatal growth. However, they found that maternal stature had limited influence on neonatal recumbent length after controlling for triceps skin folds and upper-arm muscle area (39). In our study, the association between maternal stature and childhood height remained significant even after controlling for environmental variables such as diarrheal prevalence, water supply and sanitation facilities. Furthermore, the magnitude of this association increased with the child’s age. While a mother’s genetic contribution may be in part responsible for her child’s height, the differences observed between developing and developed countries may reflect poorer nutrition and higher rates of infection. Therefore, to achieve growth comparable to developed countries, correction of childhood stunting may take several generations (40).

In summary, we found that diarrhea in the first 6 months of life was associated with shorter stature. Still to be determined is whether these effects have greater consequences in more malnourished populations. Interventions that target childhood diarrhea during the first 6 months of life are likely to prevent height faltering and its associated long-term adverse consequences, such as poor cognitive and physical development.

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