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Original Research Article

Influence of Helminth Infections on Childhood Nutritional Status in Lowland Bolivia

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ABSTRACT Infectious disease, such as diarrheal disease, respiratory infections, and parasitic infections, are an important source of nutritional and energetic stress in many populations. Inspired by the research and methodological innovations of A. Roberto Frisancho, this work considers the impact of childhood environment and local disease ecology on child health and nutritional patterns among an indigenous group in lowland Bolivia. Specifically, we examine the association between soil-transmitted helminth infection, especially hookworm species, and anthropometric markers of short- and long-term nutritional status. Fecal samples, anthropometric dimensions, and health interviews were collected for 92 children ranging in age from 2.0 to 10.9 years. Microscopic examination revealed high levels of parasitic infection, with 76% of children positive for hookworm species infections (77% of girls and 74% of boys). Less common infections included *Ascaris lumbricoides*, *Trichurius trichiura*, and *Strongyloides stercoralis* with only 15% of children positive for multiple-species infections. After adjusting for sex and age, no statistically significant associations were observed between helminth infections and the frequency of reported illness or anthropometric measures of nutritional status. These data demonstrate the difficulty of assessing nutritional impacts of endemic infections. Am. J. Hum. Biol. 21:651–656, 2009.

Infectious diseases, such as diarrheal disease, respiratory infections, and parasitic infections, are an important source of nutritional and energetic stress in many populations. Although they rarely cause death, parasitic infections, such as the soil-transmitted helminth worms, have received research attention for their capacity to subtly impact nutrition, growth, cognitive development, and lifelong health of humans (Crompton and Nesheim, 2002). Intestinal parasites are among our oldest pathogens and represent a nearly continual infection for the majority of human and nonhuman primates. Even in the absence of overt disease, long-lived helminth infections may cause chronic immune activation and nutritional stress associated with poor growth patterns (Crompton and Nesheim, 2002; Stephenson et al., 2000). Classified as "neglected diseases," research on helminth infections has recently reestablished their significance as a public health problem (Hotez et al., 2008a; Mascie-Taylor and Karim, 2003). This work considers the importance of these common infections for childhood health and nutritional status in an indigenous group in lowland Bolivia.

The term soil-transmitted helminth refers to a group of roundworms (class Nematoda) that are transmitted from person to person through contact with fecally contaminated soil. This group includes *Ascaris lumbricoides*, *Trichuris trichiura*, the hookworm species (*Ancylostoma duodenale* and *Necator americanus*), and *Strongyloides stercoralis*. Infections are concentrated in poor rural populations throughout sub-Saharan Africa, Asia, and the Americas (Hotez et al., 2008a). Within Latin America, an estimated 19% of people have trichuriasis (100 million cases), 16% ascariasis (84 million cases), and 10% are positive for hookworm infection (50 million) (de Silva et al., 2003; Hotez et al., 2008b).

The nearly universal distribution of helminth infections and relatively low levels of morbidity has led to both professional and local acceptance of worm infections as normal and unavoidable. "Worms are our life" is the response Geissler (1998) received in attempting to understand perceptions of worms among a rural population in Western Kenya. Because of this, many individuals remain chronically infected but with no clear symptoms of disease.

Although causes of malnutrition are multifactorial, helminth infections have been associated with impaired growth (Stephenson et al., 1993; Stoltzfus et al., 1997) and stunting (Casapía et al., 2006) in diverse populations. There are several mechanisms by which intestinal parasitism may cause or aggravate malnutrition including impaired nutrient absorption resulting from infection and reduced appetite (Crompton and Nesheim, 2002; Mata et al., 1977). Adult helminth worms residing in the small intestine are in an excellent position to interfere with their hosts' nutrition and can induce damage to the intestinal mucosa that may reduce a person's ability to extract and absorb nutrients from food. Helminth infections can cause vomiting, diarrhea, anorexia, abdominal pain, and nausea that may result in reduced food intake, thereby further reducing nutrient availability (Stephenson et al., 1993,

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2000). The most significant cause of nutritional stress resulting from helminth infections is hookworm-associated iron deficiency anemia. Stoltzfus et al. (1997) have estimated that light hookworm infection of 20–50 adult worms can result in significant iron losses. Even mild to moderate intensity helminth infections during childhood have been associated with undernutrition and reduced physical fitness (Ezeamama et al., 2005; Wilson et al., 1999).

This work is inspired by A. Roberto Frisancho's research on human adaptation in complex environments. Through methodological developments, he emphasized the importance of considering multiple assessments of body composition including height, skinfolds, and arm muscle area (AMA) in order to assess nutritional status and energetic reserves for growth (Frisancho, 1990, 1990). By considering a broad functional definition of adaptation, he demonstrated how these methods could be used to document the role of plasticity and developmental acclimatization in response to a broad range of adverse environmental conditions (Frisancho, 1993). This work considers the impact of childhood environment and local disease ecology on child health and nutritional patterns in lowland Bolivia. Specifically, we focus on the impact of helminth parasites on markers of short- and long-term nutritional status and the frequency of self-reported illness in childhood. We consider the impact of the most common helminth, the hookworm species, and the occurrence of polyparasitic infections.

BACKGROUND AND METHODS

Background

Research was conducted among the Tsimane', an indigenous group of ~8,000 individuals living in the Beni Department of the Bolivian Amazon. As one of the largest indigenous groups of lowland Bolivia, the Tsimane' are experiencing both the risks and benefits associated with integration into the national and international economy. Recent ethnographic works have provided a discussion of Tsimane' history and oral traditions (Huanca, 2008) and ethnobotanical knowledge (Reyes-Garcia, 2001); therefore, we limit this discussion to research focused on nutritional status and health.

As is true for much of rural South America, few Tsimane' have access to basic sanitation, electricity, or potable water. As a result, infectious disease is a widely documented health concern in the area (Byron, 2003; Gurven et al., 2007; McDade et al., 2005). For example, Byron (2003: 181–186) found that 47% of people in her sample reported some form of illness had occurred within a 1-week period. Gastrointestinal illness was responsible for 26% of illness reported among children and 15% of those reported for adults (Byron, 2003: 186). Malaria is currently not present in this region of Bolivia; however, other important infectious diseases include tuberculosis and leishmaniasis. With respect to parasitic infection, previous research has documented that over 60% of adults and children remained positive with helminth parasites over a 5-month period with no significant differences in infection rates between the wet and dry seasons (Tanner, 2005). Poor health is commonly treated with a mix of local and pharmaceutical treatments, but individuals often treat gastrointestinal illness first with traditional medicine (Calvert et al., 2008).

Consistent with the findings from other South American populations, Tsimane' have a high degree of childhood linear growth retardation and short adult stature (Hodge and Dufour, 1991; Godoy et al., 2005), a pattern which may partially result from frequent exposure to infectious disease. Although Tsimane' boys and girls are shorter and leaner than their US peers, levels of body fatness and arm muscularity (AMAZ) do not indicate severe, acute nutritional stress (Foster et al., 2005). Nutritional analysis at the household level also suggests adequate protein and calorie consumption (Godoy et al., 2005; Leonard et al., n.d.). In contrast, frequent exposure to infections disease and continual immune system activation has been associated with growth-faltering. McDade et al. (2008) demonstrated a negative relationship between immune system activation, assessed through elevated C-reactive protein levels, and linear growth in Tsimane' children.

Data collection

The project occurred in conjunction with the Tsimane' Amazonian Panel Study, an on-going study designed to investigate the impact of markets on Tsimane' health and well-being. In this project, an effort was made to recruit every individual in four research communities. The communities were selected to capture a range of variation in geographic distance from the town of San Borja, the regional commercial center in the area (pop ~19,000). Participating communities also captured a range of variation in household wealth, adult education, and access to basic sanitation including latrines and household water sources. During March 2003 to January 2004, lifestyle and health interviews were conducted among 43 households. In addition, anthropometric measurements and a single fecal sample were collected for all participating children. The study protocol was approved by the Tsimane' Grand Council and the University of Michigan Institutional Review Board for research involving human subjects.

A total of 105 children ranging in age from 2.0 to 10.9 years participated in some aspect of the study. Complete data on household conditions, anthropometric measurements, and a parasitological sample was available for 92 of these children (57% female; $n = 53$). The larger sample represents 64% of children between the ages of 2.0 and 10.9 in the research communities. Missing data occurred when households traveled out of the community for a period overlapping with a portion of data collection. Household surveys were conducted with the male and female head of each household and included sociodemographic, economic, and illness data. Parents, usually the mother, were asked to report any illness each child had experienced in the previous 14 days. Age was obtained by asking parents to list the ages and dates of birth of each child. When exact dates were unknown, ages were estimated through demographic interviews asking all adults in the household to discuss birth order for each child. Following the completion of the survey, a local nurse assisted with the collection of anthropometric measurements and a single fecal sample for parasitological analysis from each participant.

Anthropometric dimensions including height (cm), weight (kg), mid-upper arm circumference (cm), and skin fold measurements (mm) were collected using the procedures outlined in Lohman (1988) and Frisancho (1990). Children were measured barefoot and in light clothing. Mid-arm circumference was measured to the nearest millimeter using a plastic tape measure. Skinfold thickness at the triceps, biceps, subscapular, and suprailiac sites were measured to the nearest 0.5 mm using

TABLE 1. Prevalence of helminth and protozoan infection among 92 Tsimane' children 2.0–10.9 years of age

Genus or species	*n*	Percentage
Ascaris lumbricoides	6	7
Trichuris trichiura	5	5
Ancylostoma or Necator	70	76
Strongyloides stercoralis	5	5
Entamoeba coli	48	52
Giardia lamblia	1	1
Iodamoeba butschlii	8	8
Chilomastix mesnili	4	4
Polyparasitic infections		
0 species	21	23
1 species	57	62
2 or more species	14	15

TABLE 2. Descriptive statistics for sample of 2.0–10.9-year old Tsimane' children (mean and standard deviation)

Age (years)	2.0–4.9	5.0–10.9	Total
N	39	53	92
% female	62	55	58
Height for age *z*-score	−1.84 (1.52)	−1.83 (1.40)	−1.84 (1.45)
Weight for age *z*-score	−1.03 (1.37)	−0.87 (0.94)	−0.94 (1.14)
Weight for height *z*-score	0.19 (1.12)[a]	0.65 (0.57)[a]	0.44 (0.81)
Arm muscle area (mm)	13.72 (2.22)[a]	19.65 (3.24)[a]	17.13 (4.09)
Arm muscle area *z*-score	−0.32 (0.82)	−0.33 (0.72)	−0.33 (0.76)
Sum of two skinfolds (mm)	15.15 (3.85)	14.14 (4.20)	14.57 (4.07)
Sum of two skinfolds *z*-score	−0.49 (0.46)	−0.59 (0.41)	−0.55 (0.42)
Number illnesses (previous 14 days)	0.84 (0.64)[a]	0.59 (0.53)[a]	0.70 (0.59)

[a]Differences between age groups are statistically significant at $P < 0.05$.

Lange calipers. Anthropometric measurements were standardized into sex-specific *z*-scores for height-for-age (HAZ), weight-for-age (WAZ), weight-for-height (WHZ) in EpiInfo (Version 3.2) relative to the CDC/WHO 1978 reference curves recommended for international use (Hamill et al., 1979; World Health Organization, 1986). In addition, AMA was calculated from the arm circumference and triceps skinfold measurements, based on the procedure outlined by Frisancho (1990). *Z*-scores of AMA (AMAZ) and sum of triceps and subscapular skinfolds (ZSumskin) were calculated relative to the Frisancho (1990) norms, derived from the combined USNHANES I and II data sets.

A single fecal sample is commonly used to assess parasitic infection status in field surveys (Garcia, 2001). After explaining the study and obtaining consent, willing individuals were provided with a sample container and instructions to bring a fecal sample to the research house. Immediately after collection, a portion of each sample was preserved in 10% formalin following manufactures instructions (ParaPack, Meridian Diagnostics). The preserved portion was taken to La Paz for microscopic analysis (SELADIS laboratory—Servicio de Laboratorio de Diagnóstico e Investigación en Salud). Preserved samples were concentrated using the formol–ether acetate concentration procedure following WHO guidelines (1991). Individuals were considered positive for a species of gastrointestinal parasite if the diagnostic stages (eggs or cysts) were observed in the sample during microscopic analysis. An individual was considered to have a polyparasitic infection if they were found to be positive for more than one species. Subjects were divided into three groups: uninfected, infected with a single species, and infected with two or more species of intestinal helminth.

Statistical Analysis

All statistical analyses were conducted with STATA (Version 10 for Windows). The sample of 92 children did not differ from the larger panel study in terms of anthropometric measurements of nutritional status. To test the hypothesis that helminth infections are associated with stunting and reduced energetic reserves for growth, we examined the bivariate associations using two-tailed *t*-tests between the most common helminth parasite, hookworm, and anthropometric indices of short- and long-term nutritional status. One-way ANOVA was used to examine the relationship between anthropometry and the presence of polyparasitic infections. In addition, we examined the differences between infected and uninfected children by sex and age category (2–5.9 years and 6–10.9 years). Finally, in order to examine the relationship between helminth infections and other illnesses, we repeated the analyses with the number of reported illness in the previous 14 days.

RESULTS

Frequency of parasitism

High overall levels of infection were found with 77% ($n = 71$) positive for some form of helminth or protozoan infection. Table 1 summarizes the infection rates in this sample. The most common soil-transmitted helminth infection was hookworm (*Necator americanus* or *Ancylostoma duodenale*) with an overall prevalence of 76% ($n = 70$). *Ascaris lumbricoides* (7% positive), *Trichuris trichiura* (5% positive), and *Strongyloides stercoralis* (5%) were also present in much lower frequencies, often in combination with other helminths. Protozoan infection was frequent with 57% of children positive for some form of intestinal protozoa or flagella ($n = 52$). The most common protozoan infection was the nonpathogenic *Entamoeba coli* with an overall prevalence of 52%. Other protozoans encountered at a low frequency include *Iodamoeba butschlii, Chilomastix mesnili*, and *Giardia lamblia*. Although diarrhea is a common health complaint, no cases of the highly pathogenic *E. histolytica* were detected during microscopic examination. Polyparasitism was relatively uncommon in this sample, with only 15% of children harboring infections with two or more species.

Hookworm infections were common in both sexes and throughout childhood. When split by sex, 74% of boys and 77% of girls were positive for hookworm infection. Although hookworm infections were slightly more common among older children ages 6.0–10.9 (81% positive) than younger children ages 2.0–5.9 (69% positive), these age differences were not statistically significant (chi-square = 1.74; $P = 0.19$).

Parasitism and nutritional status

Table 2 contains information on body composition and frequency of reported illness among this sample. Consistent with the previous research, Tsimane' children are short and light for their age, with 51% ($n = 49$) of the sample classified as stunted with a *z*-score lower than −2 compared to US reference population (mean HAZ = −1.84). Mean weight-for-age *z*-scores are nearly one standard deviation below their US counterparts

TABLE 3. Comparison of measures of growth and nutritional status between parasitized and nonparasitized children (mean and standard deviation)

	Hookworm			Polyparasitism			
	Uninfected (n = 22)	Infected (n = 70)	P^a	0 species (n = 21)	1 species (n = 57)	>2 species (n = 14)	P^b
Height for age (z)	−1.67 (1.80)	−1.89 (1.33)	0.56	−1.65 (1.84)	−1.88 (1.43)	−1.90 (0.73)	0.82
Weight for age (z)	−0.91 (1.42)	−0.94 (1.04)	0.91	−0.89 (1.45)	−0.97 (1.13)	−0.88 (0.57)	0.95
Weight for height (z)	0.21 (0.92)	0.51 (0.87)	0.19	0.21 (0.92)	0.47 (0.93)	0.67 (0.55)	0.32
Arm muscle area (z)	−0.36 (0.95)	−0.32 (0.69)	0.80	−0.35 (0.97)	−0.28 (0.70)	−0.51 (0.63)	0.59
Sum of skinfolds (z)	−0.18 (0.92)	−0.44 (0.49)	0.09	−0.21 (0.94)	−0.40 (0.53)	−0.54 (0.33)	0.29
Number illnesses (previous 14 days)	0.95 (0.59)	0.65 (0.59)	0.19	0.50 (0.59)	0.69 (0.60)	0.50 (0.52)	0.24

[a]*P*-value of two-tailed *t*-test.
[b]*P*-value of one-way ANOVA.

(mean WAZ = −0.94). In contrast, weight-for-height scores compare more favorably with US references (mean WHZ = 0.44). Only 2% (n = 2) of this sample of Tsimane' children would be classified as wasted with a HAZ score less two standard deviations below the US mean. Weight-for-height z-scores are significantly higher in older children ($t = -2.47$; df = 90; $P = 0.016$).

Standardized measures of body fatness indicate that Tsimane' children are leaner than the US reference population, but not sufficiently so as to indicate severe energy stress (mean ZSumskin = −0.55). In addition, AMAZ of Tsimane' children indicate that they are not experiencing acute protein malnutrition (mean AMAZ = −0.33). Although older children appear to have greater AMAZ ($t = -9.83$; df = 90; $P < 0.00$), when standardized by age (AMAZ) these differences disappear ($t = 0.04$; df = 90; $P = 0.96$). Finally, there are no significant differences between males and females within age groups in this sample (results not shown).

To assess the frequency of acute illness, we rely on illness recall surveys. Acute illness is very common with 61% of children reporting at least one illness in the previous 14 days (Table 2). The most commonly reported illnesses were respiratory infections, including colds, and intestinal illnesses such as stomach pain and diarrhea. Although acute illness is common, only six children (7%) reported more than one illness as reflected in a low mean number of illnesses. There were no differences between males and females in the number of reported illnesses but younger children aged 2.0–4.9 were reported to have significantly more illnesses than older children aged 5.0–10.9 ($t = 2.04$, df = 90; $P = 0.04$).

In the entire sample of 2.0–10.9-year-olds, helminth infections are not significantly associated with anthropometric indices of long-term nutritional status (HAZ) or short-term energetic reserves including skinfold measurements of body fatness or AMAZ. Table 3 presents associations between anthropometric indices of nutritional status and the presence of hookworm infections and polyparasitic infection. Although children who were positive for hookworm infection had lower mean values of HAZ, WAZ, and HAZ scores than children who were negative for hookworm infection, the differences between the two groups are not statistically significant. With regard to AMAZ and body fatness (ZSumskin), a similar pattern of slightly lower values in hookworm-infected individuals was observed but failed to achieve statistical significance. Comparisons between infected and uninfected children in each age group produced similarly nonsignificant differences in anthropometric indices (results not shown).

Results were similar with respect to the occurrence of polyparasitic infections. Children who were positive for two or more species had lower mean values of Height for Age, AMA, and sum of two Skinfolds than uninfected children or those positive for one species, although the differences were not statistically significant. It is interesting to note that the number of reported illnesses also did not vary with the number of helminth species harbored by the child.

DISCUSSION AND CONCLUSIONS

The soil-transmitted helminths are among our oldest pathogens and remain an important part of infectious disease in many of the world's poorer, more vulnerable populations. This work has evaluated the relative impacts of helminth infections on childhood height, weight, and energetic reserves in the form of body fat in an environment where such infections are common. Seventy-seven percent of children aged 2.0–10.9 were positive for some form of intestinal parasite, with the most common being the hookworm species. A high prevalence of infection is consistent with previous findings among a sample of older Tsimane', where nearly 90% of adolescents and adults were found to harbor some form of gastrointestinal parasite and 77% were positive for hookworm (Tanner, 2005). In both cases, the frequency of helminth infection is high but most individuals were infected with only one species. A high prevalence of intestinal parasites is consistent with what is found throughout indigenous populations in the rural tropics (Hurtado et al., 2005).

The negative consequences of helminth infections have been documented in diverse populations (Jardim-Botelho et al., 2008; Stoltzfus et al., 1997; Wilson et al., 1999), but the results are merely suggestive here. Although the pattern found in our data is in the expected direction, there are no statistically significant associations between the most common parasitic infection, hookworm, and either long-term markers of growth (HAZ) or short-term indicators of energetic reserves of nutritional stress (Skinfold measurements or AMA *Z*-score). Results are similar for multiple species infections and the results remain when controlling for age and sex.

There are several possible explanations for these findings. First, a weakness of this study is a relatively small sample size compounded by a high frequency of helminth infections within the sample. It is quite plausible that all Tsimane' children are faced with nearly unavoidable exposure to the infectious stages of gastrointestinal parasites through their childhood. In addition, hookworm, the most commonly encountered parasite in this sample, is often associated with anemia in short-term infections. However, chronic moderate to heavy intensity hookworm infections has been associated with chronic anemia and growth retardation in children (Crompton and Nesheim, 2002). Previous research among Tsimane' has found that hookworm infections appear to be endemic year-round in the area suggesting that children would be continually infected and reinfected throughout childhood. Therefore, it is possible that a larger sample containing uninfected children or a longitudinal study may be necessary to capture the nutritional consequences of infection.

A second possibility is that, although infections are frequent, social and cultural practices are effective at reducing the occurrence of symptoms and overt disease associated with infection. Gastrointestinal illness, diarrhea, and parasites are often initially treated with botanical cures commonly found in household gardens. Among the Tsimane', McDade et al. (2007) found that increased levels of maternal ethnobotanical knowledge is associated with better child health including height, skin-fold measurements, and reduced levels of C-reactive protein. Although acknowledging that ethnobotanical knowledge is multifaceted, they rely on a series of interview-based methods to quantify individual knowledge of local plant use. Future studies are needed to directly assess ethnomedical knowledge, but it is possible that parents who have richer general ethnobotanical knowledge may be better able to translate the knowledge into behaviors or practices that result in either more effective treatment of childhood disease, increased ability to avoid infection, or both. In this context, the occurrence of disease, illness, and physical manifestations of infection may result both directly and indirectly from a breakdown in social, ecological, or economic conditions.

A final possibility is that the high frequency of stunting and slow growth represents a developmental acclimatization, or more precisely an accommodation, to the synergistic effects of nutrition and disease stressors throughout childhood. Several studies among rural populations have failed to find a nutritional impact of gastrointestinal parasitism (Marini et al., 2007; Northrop-Clewes et al., 2001). In Venezuela, Marini and colleagues (2007) found no detrimental effects of gastrointestinal parasites on nutrition status and body morphology. In rural Bangladeshi children, low-intensity helminth infections were also found to not contribute significantly to the poor growth of children (Northrop-Clewes et al., 2001). In disadvantaged societies facing the combined stressors of malnutrition and frequent exposure to infectious disease, early exposure to gastrointestinal parasites may modify or prime immune response in children, which may serve to buffer the consequences of more acute infections.

The results of this work on helminth infections, although based on a cross-sectional sample, raise important questions about the multifaceted causes of poor health among indigenous South American populations. Hurtado et al. (2001, 2005) note that indigenous South American populations tend to be chronically infected with soil-transmitted helminth infections and simultaneously produce very high levels of immunoglobulin E. They argue that this may result in unique immunological and physiological vulnerabilities to disease stress. If this hypothesis is shown to be true, it will require a revision of our interpretations of normal and abnormal physiological functioning across diverse environmental conditions. This research reinforces the need for continued investigations into understudied problems of rural and indigenous health throughout South America.

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