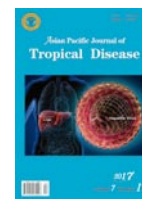


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Nutritional status of children with vivax malaria in the Amazon Basin

Rosa Maria Dias¹, José Luiz Fernandes Vieira^{2*}, Bianca da Conceição Cabral¹, Ana Maria Revoredo da Silva Ventura³, Paula Valente Leão¹, Laélia Maria Barra Feio Brasil⁴, Marcieni Ataíde de Andrade²

¹Nutrition Faculty, Health Science Institute, Para Federal University, Para, Brazil

²Pharmacy Faculty, Health Science Institute, Para Federal University, Para, Brazil

³Malaria Ambulatory, Evandro Chagas Institute, Para, Brazil

⁴Medicine Faculty, Health Science Institute, Para Federal University Para, Brazil

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ABSTRACT

Objective: To investigate the nutritional status of children and adolescents with *Plasmodium vivax* malaria who live in an endemic area with unstable transmission in the west of the Amazon Basin. Moreover, we sought to evaluate if the nutritional status influences the parasitemia at admission and the history of malaria.

Methods: Nutritional indexes used were height-for-age, weight-for-age, and body mass index-for-age and children were classified according national and regional parameters based on Z scores of the World Health Organization.

Results: A total of 43 children and 18 adolescents were enrolled in the study. Most of participants were eutrophic, but there is a high proportion of linear growth deficits in both children and adolescents, compared to national or regional standards. The history of disease and the parasitemia at admission were not associated with height-to-age in both age groups.

Conclusions: Malaria by *Plasmodium vivax* can corroborate to deficit in linear growth of children.

1. Introduction

Malaria is a relevant public health issue in several countries[1]. In Brazil, approximately 146000 episodes of the disease were reported in 2015 and most of the cases have occurred in the Amazon Basin (99.9%). *Plasmodium vivax* (*P. vivax*) was the predominant species as it has accounted for 85% of cases. The disease affected equally all age groups and both genders[2]. In endemic areas, such as in the Brazilian Amazon Basin, only a few cases of vivax malaria evolve to severe illness and most of the patients have mild signs and symptoms and low parasitemia. Overall, the partial immunity resulting from repeated episodes of malaria and the easy access to diagnosis and treatment prevents the occurrence of severe cases[3,4].

In children, the repeated episodes of the disease are common, causing a negative impact on the immune and hematopoietic systems, cognition and nutritional status[5-8]. The relation between malaria and nutritional status is controversial and complex once nutritional status influences the immune response to infection whereas the infection directly influences the nutritional status. Some studies have not found associations between the disease and the nutritional status whereas others have shown that the poor nutritional status has a significant impact on the morbidity and mortality due to malaria[9-12].

In Latin America, only a few studies evaluated the nutritional status of children with malaria and, only recently, the nutritional status of children with *P. vivax* malaria was associated with the disease in a prospective study in Western Amazon[10]. In a recent study, our research team has found significant changes in lipid levels of children in the acute phase of *P. vivax* malaria, which may occur with the poor nutritional status[13]. Thus, the aim of the current paper was to investigate the nutritional status of children and adolescents with *P. vivax* malaria who live in an endemic area with unstable transmission in the west of the Amazon Basin. Moreover, we sought to evaluate if the nutritional status influences the parasitemia at admission and the history of malaria.

*Corresponding author: José Luiz Fernandes Vieira, School of Pharmacy, Para Federal University, Augusto Correa Street 01, Belem, Zip code: 66075-740, Para, Brazil.

Tel: +559132017733

E-mail: jvieira@ufpa.br

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2. Materials and methods

2.1. Study site and participants

The study is a component of a research project designated to evaluate health conditions of inhabitants of the Marajo Island. Although the Marajo Island is considered the largest fluvial island with a high touristic activity, most of the inhabitants live below the poverty line with most municipalities showing low economic status. The study was carried out from January to December 2014 in the municipality of Anajas (00°59'21" S and 49°56'24" W) in the State of Para. The municipality has 28 012 inhabitants, of which 7 347 are children aged 2–10 years. In 2014, the disease occurred in approximately 36.6% of these children. The annual incidence of cases is sustained above 50/1 000 inhabitants, with the prevalence of *P. vivax* (86.3%).

Participants were randomly recruited amongst those who spontaneously searched for attendance at health facilities of the municipality with suggestive signs and symptoms of malaria, with posterior confirmed blood smears as positive mono infection by *P. vivax*. Exclusion criteria included patients with mixed infection or signs and symptoms of severe disease (jaundice, renal or pulmonary impairment, severe anemia, altered level of consciousness), chronic and other parasitic diseases mainly including gastrointestinal helminth and who has reported a history of malaria infection within the previous three months.

The participants of the study were treated with chloroquine and primaquine, following the recommendation of the World Health Organization (WHO), with primaquine doses adjusted for weight[14].

2.2. Data collection

The guardians of children and adolescents answered a clinical questionnaire before the inclusion in the study. The data recorded were age, gender, scholar degree, ethnicity, history of malaria, parasitemia at admission and the uses of prophylactic measures.

2.3. Nutritional evaluation

Nutritional evaluation was done at admission using anthropometric measures. Weight was measured using a digital weight scale with ± 100 g error margin. The mean value of three measures was considered the children's weight. The height was estimated with a stadiometer with scale in centimeters. The age was reported by guardians of the patients enrolled in the study. Body mass index was calculated using the ANTHRO and ANTHRO PLUS programs. The indexes height-for-age, weight-for-age, and body mass index-for-age were used to classify the nutritional status, which was based on the Z scores in accordance with the World Health Organization (WHO) growth reference curves. Underweight was defined as a weight-for-age Z score of < -2 and stunting as height-for-age Z score of < -2 . The Z scores of < -3 indicated severe underweight or severe stunting[15-17]. The values found were compared to national and regional standard of the Ministry of Health of Brazil[18].

2.4. Parasite count

Parasite count was performed according to the Walker technique. A microscopist using 100 \times (oil immersion) objectives examined blood films and recorded the number of parasites per 200 white blood cells. The limit of detection of parasites was 40/ μ L[19].

2.5. Data analysis

Data are shown as frequencies of occurrence. Qualitative variables were compared between groups of study by *Chi*-squared test (χ^2), *G*-test and Fischer exact test. All *P*-values were two-tailed, and *P* < 0.05 was considered significant. Statistical analyses were performed with Statistica software package (Version 7.0, Stat Soft Inc. 2004, Tulsa, USA).

2.6. Ethical statement

The study was submitted to Plataforma Brasil under protocol CAAE 2 07199612.0.0000.0018 and approved by the Ethical Comite of Health Science Institute of Para Federal University under the number 261.593/2013.

3. Results

A total of 61 patients were enrolled in the study. Amongst the patients, 43 (70.5%) were children and 18 (29.5%) were adolescent. Most of the patients were male (67.2%) and were enrolled in schools (60.7%). The occurrence of more than 4 episodes of the disease was reported by 57.4% of all participants of the study. Parasite density below 10 000 mm^3 was found in the majority of patients (77.1%). The baseline characteristics are in Table 1.

Table 1
Baseline characteristic of participants.

Variables	<i>n</i>	%	<i>P</i> value
Gender			
Male	41	67.2	0.01
Female	20	32.8	
Age group (years)			
2–5	28	45.9	0.08
6–9	14	22.9	
10–16	19	31.2	
Scholar degree			
Not started	24	39.3	
Preschool	2	3.3	< 0.01
1st to 4th grade	23	37.7	
5th to 8th grade	12	19.7	
History of malaria, number of episodes			
Primo-infection	5	8.2	
1–3	21	34.4	$< 0.000 1$
> 4	35	57.4	
Parasitemia at admission			
$< 10 000 \text{ mm}^3$	47	77.1	$< 0.000 1$
$> 10 000 \text{ mm}^3$	14	22.9	

Most of the patients enrolled in the study having height-for-age, body mass index-for-age, and weight-for-age z distribution within the normal range according to national and regional standards. Underweight was found in 7.0% of children and overweight was

found in 5.6% of the adolescents (Table 2). Low height-for-age was found in 25.6% of the children and 22.2% of the adolescents. The height-for-age was not associated with parasitemia at admission or with the number of previous episodes of the disease in both age groups. In children with poor nutritional status, the history of the disease and parasite count below 10000 mm³ was predominant. For adolescents of the same group, the occurrence of more than four episodes of the disease was predominant, but the parasite count was similar in both groups (Table 3).

Table 2

Nutritional index of children and adolescents enrolled in the study.

Nutritional index	Values		
	n	%	P values
Children			
Height-for-age (Z scores)			
< -2	11	25.6	0.002
≥ -2 e ≤ +2	32	74.4	
Weight-for-age (Z scores)			
< -2	3	7.0	< 0.001
≥ -2 e ≤ +2	40	93.0	
Adolescents			
Height-for-age (Z scores)			
< -2	4	22.2	0.02
≥ -2 e ≤ +2	14	77.8	
Body mass index-for-age (Z scores)			
≥ -2 e ≤ +2	17	94.4	< 0.01
> +2	1	5.6	

Table 3

Associations between nutritional status with history of malaria and parasitemia at admission.

Variable	Children height-for-age (Z scores)			Adolescents height-for-age (Z scores)		
	< -2	≥ -2 e ≤ +2	P values	< -2	≥ -2 e ≤ +2	P values
	[n (%)]	[n (%)]		[n (%)]	[n (%)]	
History of disease, number						
Primo-infection	3 (60.0)	2 (40.0)		0	0	
1-3	4 (23.5)	13 (76.5)	0.236	0	4 (100.0)	nd
> 4	4 (19.1)	17 (80.9)		4 (28.6)	10 (71.4)	
Parasitemia at admission (mm³)						
<10000	8 (25.0)	24 (75.0)	0.99	2 (13.3)	13 (86.7)	0.107
>10000	3 (27.3)	8 (72.7)		2 (66.7)	1 (33.3)	

nd: Not determined.

4. Discussion

In the study, the nutritional status of children and adolescents with *P. vivax* malaria were assessed using anthropometrics measures, of which values are related to genetic and environmental characteristics[17,20,21]. The nutritional indexes derived from anthropometric measures were classified according to the regional and national standards[18]. The relation height-for-age was chosen to assess the associations of the nutritional status with the history of the disease and with parasitemia at admission since it is a more reliable estimation of a long-term impact on nutrition. Other nutritional indexes based on patient weight, such as weight-for-age and body mass index-for-age may suffer considerable changes in the acute phase of several diseases[17,20,21].

Most of the children and adolescents were eutrophic at admission, having adequate indexes of weight-for-age and body mass index-for-age. Moreover, these nutritional indexes were similar in male and

female patients of both age groups. These results suggest a low acute impact of the disease on the nutritional indexes based on the weight of patients. The probable causes are the low parasite density, the mild signs and symptoms of malaria and the short interval between the onset of signs and symptoms and the search for health attendance.

The height-for-age has normal values in most of the patients, but the proportion of linear growth deficits of 25% and 15% seen in children and adolescents is high, compared to the national or regional standards of 6.2% and 10.3% for children and 5.9% and 8.9% for adolescents of similar ages and socio-economic status, but with no history of malaria[18]. These data are in line with studies done in other endemic areas, which suggested that children living in these areas might have a deficit of linear growth[10,11,22,23].

Children with low height-for-age had a history of 1-3 episodes of malaria. Male children showed the highest proportion of linear growth deficit compared to female children, but the difference was not statistically significant. The plausible explanation is the fact that male children, since early age, have more outdoor recreational activities whereas female children grow indoors in their homes. Thus, this behavior of male children may increase the risk of contracting infectious diseases, causing a more prominent long-term impact on nutrition. Furthermore, the linear growth deficit was high in children compared to adolescents, suggesting a recovery of linear growth in most adolescents[24].

The causality of the association between malaria and deficit of linear growth has several confounding factors in the Amazon Basin, mainly in the Marajo Island, where most of the inhabitant lives in the poverty and the disease is associated with both low socioeconomic status and low educational degree of the children and of their parents. Thus, low social-economical level, the concurrent infectious diseases such viruses and intestinal parasites, as well as the deficit of macro or micronutrient may act synergistically on the nutritional status of local inhabitants[10,11,25]. Furthermore, the transversal design of the study instead of a prospective cohort study, did not allow comparisons over the time to determine the causality between poor nutritional status and malaria, which was considered the main limitation of the study.

The repetitive episodes of the disease and parasitemia at admission were not associated to deficits in linear growth in both children and adolescents. The plausible explanation for these findings was the inadequate use of a long-term nutritional index for evaluating such associations, as the use of weight-based nutritional indexes could be a potential bias because there was a high proportion of eutrophic patients in the study[17,20,21].

The results of the present study are clinically relevant as they point out the potential deficiency of linear growth in children living in endemic areas and with reports of several episodes of malaria, which are probably recovered at adolescence. This finding requires public interventions to improve the health quality of these children. Moreover, the data contribute to the comprehension of the intricate causality between malaria and nutritional status in children development.

Based on the results of the nutritional indexes, most patients were eutrophic, suggesting a low impact of the disease on the nutritional status of children and adolescents. However, there is a high

proportion of linear growth deficits in both children and adolescents, compared to national and regional standards. Finally, the history of the disease and parasitemia at admission were not associated to height-for-age.

Conflict of interest statement

We declare that we have no conflict of interest.

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