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Factors Associated with the Infection by *Plasmodium vivax* in Children and Adolescents from the Brazilian Amazon Basin

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Abstract

Objective: To investigate the factors associated with malaria vivax infection in children and adolescents from an endemic area in the Eastern portion of the Brazilian Amazon basin. **Methods:** A case-control study was carried out in the municipality of Anajas, Brazil, from January 2016 to September 2017. Questionnaires were applied to the relative or the legal tutors of children and adolescents with questions regarding social and economic status, educational degree, knowledge about malaria, and the use of protective measures against mosquito bites. Anthropometric measures were performed in children and adolescents. **Results:** A total of 58 cases and 61 controls were included in the study. Most of the participants were male, eutrophics, and their relatives presented low educational degrees as well as low social and economic status. The knowledge of malaria was limited, but the percentage of individuals using long-lasting insecticidal nets was high. The presence of peri-domiciliary breeding sites for Anopheles vector was the most critical factor for malaria. **Conclusion:** The occurrence of malaria was associated with low social and economic status, a low educational degree, the unfamiliarity with malaria and the presence of breeding sites for Anopheles mosquito surrounding individual domiciles.

Keywords

Infectious Diseases, Malaria, Epidemiology, Risk Factor

1. Introduction

Malaria by *Plasmodium vivax* remains a significant public health issue worldwide, with three billion of individuals who are at risk to contract the disease, and approximately 435,000 each year, the majority in children (61%) who are a group at risk to develop severe disease [1].

In Brazil, most of the cases (99%) occur in the Brazilian Amazon basin, which presents a non-homogenous transmission among municipalities, and *P. vivax* accounts for 85% of cases. Despite the effort of the Brazilian Health Authorities to control the disease, the incidence is still high, with 193,838 cases notified in 2018, amongst them, 45,835 (23.6%) in the State of Pará [2].

The adequate management of risk factors for malaria, such as the use of long-lasting insecticidal nets (LLIN), indoor residual spray (IRS), use of repellent, availability of mosquito breeding sites in the peridomicile and the outdoors activities overnight, contribute for reducing the burden of the disease [3] [4]. In a large endemic area with several geographical, social, and economic scenarios such as the Brazilian Amazon basin, the factors associated with malaria differ among municipalities. Moreover, they are poorly understood in children and adolescents. Therefore, the present study aims to investigate the factors associated with malaria vivax infection in children and adolescents from an endemic area in the Eastern portion of the Brazilian Amazon basin.

2. Material and Methods

2.1. Study Site and Participants

An epidemiological study of case and control was carried out from January 2016 to September 2017 with children and adolescents from Anajás in the State of Para. The municipality has an average temperature of 23.4˚C - 26.5˚C, with annual precipitation of 1437.0 - 3022.7 mm and an annual daylight duration of 1573.5 - 2443.4 hours. Anajas is located in the Marajo Island (00˚59'21"S and 49˚56'24"W) with 28,012 inhabitants, amongst them, 7337 children aged 20 - 10 years old. The municipality accounts for 10.4% of cases of malaria in the State of Para.

The participants were included in the study according to the following criteria:

Case: children and adolescents aged 2 - 14 years, both genders, with mono-infection by *P. vivax* diagnosed by microscopic examination of Giemsa-stained thick blood films, which were admitted in the study by spontaneous demand after their relatives or legal tutors have searched for the ambulatory of diagnosis and treatment of malaria of the municipality with signs and symptoms suggestive of malaria.

Control: children and adolescents aged 2 - 14 years with a negative microscopic examination of a blood smear on three consecutive occasions as well as with no recent (2 years) history of malaria recruited in two public schools of the municipality. The relative or the legal tutors of children or adolescents agreed with the participation in the study and signed the informed consent.

The criteria for the exclusion of the cases from the study were those with signs and symptoms of severe malaria (parasitemia over 5%, jaundice, pulmo-

nary or renal impairment, severe anemia, altered levels of consciousness) and self-referred glucose-6-phosphate dehydrogenase (G6PD) deficiency. Case and control with known underlying severe diseases, including congenital diseases, also were excluded.

2.2. Data Collection

Data were collected during an interview with the parents or legal tutors of the children and adolescents at their inclusion in the study. The questionnaire applied contained questions regarding social and economic status, educational degree, knowledge about malaria, and the use of protective measures against mosquito bites. The questionnaire was previously validated in a pilot study before the commencement of the study.

The following data were collected from the parents or legal tutor: 1) socio-economic status: scholar degree (years of study), marital status (stable or unstable), occupation (stable or unstable), family income (below or above 100 US$). 2) knowledge about malaria: the forms of transmission of the disease, and the use of protective measures against mosquito bites, as the use of long-lasting insecticidal nets (LLIN), indoor residual spray (IRS) and the use of repellent. 3) the presence of peri-domiciliary breeding sites for *Anopheles* vector.

The following data were collected from the children and adolescents included in this study: weight (kilograms), height (centimeters), age (years), and gender.

2.3. Anthropometric Measures

Children and adolescents were weighed with a calibrated digital weight scale (180 Kg) with a precision of 100 g (SECA™). The mean value of three measures was considered the average weight of the children. The height was obtained with a stadiometer (Alturexata®) with a scale inside.

The height-for-age, weight-for-age, and body mass index-for-age indexes were used to classify their nutritional status, which was based on the Z scores following the World Health Organization (WHO) growth reference curves [5] [6].

2.4. Sample Size

The sample size was calculated by assuming an odds ratio of 0.2 for sleeping under ITNs, control exposure of 50%, and case to control the ratio of 1:1 for a total sample size of 120. The sample size was 130. However, only 119 children and adolescents were included in the study.

2.5. Data Analysis

Data are presented as frequencies of occurrence or as median and ranges. Both bivariate and multivariable logistic regression was performed to identify factors associated with malaria. Data were analyzed using Statistical Package for the Social Sciences (SPSS) software, Release 21 (IBM Inc., Armonk, NY, USA). The accepted significance level was 5%.

2.6. Ethics Approval and Consent to Participate

This study was revised and approved by the Ethical Committee of The Health Science Institute of UFPA, Number 261.593/2013. The written informed consent was obtained from each guardian of children and adolescents.

3. Results

A total of 119 children and adolescents were included in the study, amongst them, 58 (48.7%) cases and 61 (51.3%) controls. The mean age of each group was 7.3 (4.5) years and 7.6 (4.2), respectively. Most of the study participants from both groups were male. The social and economic data of the case groups showed that most of the parents or legal tutors have an unstable occupation with a family income below 100 US, indicating a low socio-economic status. The educational degree, occupation, and family income were significant predictors for malaria (Table 1).

The long-lasting insecticidal nets (LLIN) was the most used prophylactic measure in both groups of the study. There was no report of chemoprophylaxis in both groups. Moreover, a small proportion of houses in both groups reported the use of windows networks and indoor residual spraying (IRS). A similar result was found with the individual use of repellents in both groups. These outcomes do not modify the occurrence of malaria.

The knowledge of the transmission of malaria was different between the groups and was a significant factor for malaria infection. Finally, the presence of peridomiciliary breeding sites for *Anopheles* vector was different between groups and considered the most important predictor of the disease (Table 2).

4. Discussion

The knowledge and management of factors associated with the transmission of malaria in the Brazilian Amazon basin are essential to guide the surveillance efforts to reducing the social and economic negative impact of the disease. The strategies of the Brazilian Health Authorities to reduce the burden of the disease are based on the control of Anopheles vector and in the early diagnosis and prompt treatment of cases [7]. However, geographical diversity and the extent of the Amazon basin constitute a challenge to the fight against malaria. In the Marajo Island, there are areas with intense touristic activities in the north of the island coexisting with those where the agricultural and fisher practices predominate. A substantial difference in biomes across regions is noted with most of the cases of the disease occurs in municipalities from the center to the south of the island [2].

Most of children and adolescents with *P. vivax* were from families that live in poverty receiving a monthly income below 100 US$, which is in line with data from the WHO that demonstrated that the disease concentrates in areas with low economic status in the tropical regions, where individuals present difficulty to access public health services for diagnosis and treatment of the disease as well

Table 1. Socio demographic characteristics of the study participants.

Characteristic	Case (n = 58)		Control (n = 61)		P value
	n	%	n	%	
Sex					
Male	38	65.5	36	59.0	0.5879*
Female	20	34.5	25	41.0	
Age range, years					
2 to 4	25	43.1	21	34.4	
5 to 9	14	24.1	22	36.1	0.3575**
10 to 15	19	32.8	18	29.5	
Nutritional status (A/I)					
Low	14	25.0	8	17.5	0.1895*
Appropriate	44	75.0	53	82.5	
Guardian					
Mother	52	89.7	53	86.9	0.8539*
Other	6	10.3	8	13.1	
Educational status					
No formal education	39	67.2	19	31.1	<0.0001**
Primary (1 - 8 th)	15	25.9	17	27.9	
Secundary+	4	6.9	11	18.0	
Marital status					
Married	36	62.1	42	68.8	0.5583*
Single	22	37.9	19	31.2	
Occupation					
Unstable	53	91.4	40	65.6	0.0046*
Stable	5	8.6	21	34.4	
Family income					
<100 US$	42	72.4	31	50.8	0.0258*
≥100 US$	16	27.6	30	49.2	

*Chi-square test. **G test.

as to the prophylactic measures [1]. The disease impairs the economic development of endemic areas as most of the individuals affected are in productive age, which contributes to maintaining the cycle of poverty-related to malaria [7] [8].

Poverty also contributes to the low educational degree, as most of the inhabitants of the study area change in early ages from educational activities to unstable occupational activities in order to support their families. There is a significant influence of socio-economical and educational status on the risk of malaria [9]. In the study, the low educational degree, the family income, and the unstable occupation were significant factors for malaria vivax.

Poverty and the low educational degree accompanied the unsatisfactory familiarity with the knowledge of the disease in the cases. A previous study showed that the unsatisfactory knowledge of the disease contributed to increasing the

Table 2. Factors associated with malaria infection in children.

Factors	Case	Control	COR (95% CI)	AOR (95% CI)
Sex				
Male	38	36	1.32 (0.63 - 3.78)	1.53 (0.67 - 3.46)
Female	20	25		
Age range, years				
2 to 9	39	43	0.86 (0.40 - 1.87)	0.89 (0.37 - 2.12)
10 to 16	19	18		
Educational status				
Primary (1 - 8 th)	54	36	9.38 (3.01 - 29.2)	6.11 (1.87 - 19.9)*
Secundary+	4	25		
Nutritional status				
Inadequate	14	8	2.11 (0.81 - 5.48)	2.02 (0.71 - 5.76)
Adequate	44	53		
Knowledge on malaria				
No	21	11	2.58 (1.11 - 6.0)	2.74 (1.04 - 7.24)*
Yes	37	50		
LLIN				
Yes	48	53	1.38 (0.50 - 3.78)	2.90 (0.72 - 11.71)
No	10	8		
SRI				
Yes	6	9	1.50 (0.50 - 4.52)	2.18 (0.59 - 8.02)
No	52	52		
Repellent				
Yes	8	13	1.69 (0.64 - 4.45)	0.53 (0.17 - 1.69)
No	50	48		
Mosquito breeding sites				
Yes	2	25	19.44(4.34 - 87.1)	22.48 (4.65 - 108.9)*
No	56	36		

*$p < 0.05$ in multivariable analysis. COR: crude odds ratio. AOR—adjusted odds ratio.

risk of infection [10].

There is a synergism between infection and nutrition, and children and adolescents with low nutritional status have a high probability of worsening the signs and symptoms of the disease. The deaths related to malaria in children and adolescents have been associated with undernutrition and deficiency of nutrients like vitamin A, zinc, folate, and iron, which are essential elements for the defense of the human host. However, there was no significant association between the nutritional status and the occurrence of the disease, which could be due to the high proportion of eutrophic individuals in the study groups [11] [12] [13] [14].

The use of LLIN is the principal prophylactic measure against Anopheles bite

adopted by the Brazilian Health Authorities, and the data showed a high coverage of LLIN in both study groups. Other prophylactic measures as IRS, the use of repellents, and the windows network were reported by a small proportion of individuals in the study, which could be related to the social vulnerability of the inhabitants of Anajas.

The presence of breeding sites for Anopheles mosquito in the peridomicile was the most critical factor for malaria infection. These sites result from the inappropriate discharge of domestic residues, which creates a small collection of water that suffers the action of the tide in the rainy season, being dissipated by the Anajas River. However, in the dry season, these small collections of water constitute a suitable site for the breeding of the Anopheles vectors. Thus, the cases of malaria decrease in the rainy season and begin to increase in the transition of rainy to dry seasons [15].

The limitation of the study was the reduced number of participants due to the difficulties of including individuals in the control group. However, there was a similar distribution of participants between the study groups.

5. Conclusion

Malaria occurs in children and adolescents of both genders. The low social and economic status of their families are significant predictors of the disease. These factors impact the educational degree of the guardians leading to the unfamiliarity with the disease. Finally, the presence of breeding sites for Anopheles mosquito surrounding individual domiciles is a significant factor for the disease.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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