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Research Article

Overweight and Obesity as Protective Factors for Clinical Manifestations in *Vivax* Malaria

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Abstract

Introduction: Little is known about the relationship of nutritional status with the medical study of infectious diseases, especially malaria. The aim of this study is to investigate the clinical features of patients with *P. vivax* malaria in relation to their nutritional status.

Methods: A retrospective study of the medical records of 94 adults with uncomplicated *P. vivax* malaria was conducted in the Evandro Chagas Institute in Ananindeua city, Brazil, between 2010 and 2011. The research protocol included identification data, previous history of malaria, weight, height, parasitemia and clinical manifestations. A score ranging was determined in accordance with the intensity of the symptoms.

Results and Discussion: Findings from the Spearman linear correlation to analyze the relationship between the nutritional status and the clinical score was shown to be negative of all the individuals (rs = -0.24, p = 0.02), in individuals who were not history of malaria (rs = -0.32, p = 0.03), in individuals who were low parasitaemia (rs = -0.37, p = 0.002) and becomes more evident among these individuals infected for the first time (rs = -0.49, p < 0.001).

Conclusion: Overweight and obesity represent a protective factor for the clinical manifestations of *P. vivax* malaria with low parasitemia, in patients infected for the first time. The present findings increase our understanding about the obesity and overweight in malaria.

Keywords: Body mass; Obesity; Malaria; *Plasmodium vivax*

Abbreviations

BMI: Body Mass Index; NS: Nutritional Status; CS: Clinical Score

Introduction

Malaria is a public health problem in many parts of the world, and it is responsible for about 600,000 human deaths per year. In Brazil, the largest number of cases is recorded in the Amazon region (99.9%), where the disease can be classified into three species: *Plasmodium vivax* (more than 80%), *P. falciparum* (15%), and *P. malariae* (less than 1%). Mixed infections, especially by the association of *P. vivax* and *P. falciparum*, are also observed [1]. The clinical manifestations of malaria are directly related to the individual's specific level of immunity to the parasite and the strain causing the infection [2].

Little is known about the relationship of nutritional status with the medical study of infectious diseases, especially malaria. In the literature, there are few studies correlating the clinical manifestations of *P. vivax* malaria in adult subjects with nutritional status, especially for those with obesity [3]. The aim of this study is to investigate the clinical features of patients with *P. vivax* malaria in relation to their nutritional status.

Materials and Methods

A retrospective study, observational and includes a cases series of the medical records of adults with uncomplicated *P. vivax* malaria, whose diagnosis and clinical-parasitological follow-up was conducted in the Laboratory for Malaria Clinical Trials at the Evandro Chagas Institute in Ananindeua, Pará, Brazil. Between 2010 and 2011, there were 94 records included of patients aged 18-59 years of age with a positive thick blood smear for *P. vivax*. The research protocol included identification data, previous history of malaria, weight and height and parasitaemia at the time of diagnosis (D0), as well as clinical manifestations.

A score ranging from zero to three was determined in accordance with the intensity of the symptoms (0 = absent, 1 = mild, 2 = moderate, 3 = severe) displayed by the patient at the time of diagnosis, so that the total score for fever, chills, headache, arthralgia, myalgia, asthenia, back pain, abdominal pain, and nausea ranged between 0 and 27 points. The parasitaemia was quantified in mm^3, being classified as low if less than 10,000 parasites/mm^3, and high if equal to or greater than 10,000 parasites/mm^3. The parasitemia levels had been transformed into Ln, presenting a normal distribution. The Body Mass Index (BMI) was used to assess the nutritional status of individuals with malaria: eutrophic/normal weight (18.5 < BMI < 24.9); overweight (25 < BMI < 29.9); and obese (BMI ≥ 30). Thus, for each nutritional group was performed the 1:1 proportion (primary history patient: previous history patient).

The study was approved by the Research and Ethics Committee of the Evandro Chagas Institute (no. 0015/10 CAAE: 0015.0.072.000-10). The data were recorded in the EPIINFO 7.3.5 program. Statistical analysis was performed in the Biostat 5.0 Program. ANOVA, Kruskal-

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Table 1: Distribution of nutritional groups in relation to age, height, weight, parasitaemia and clinical score.

Characteristics	General (N=94)	Nutritional status			P value*
		Eutrophic (*n*=40)	Overweight (*n*=40)	Obese (*n*=14)	
Age (years)	34.9	30.3	38.2	39.0	< 0.01
Height (m)	1.6	1.6	1.6	1.7	0.16
Weight (kg)	71.6	61.3	74.0	94.8	< 0.01
Parasitaemia (Ln)	8.2	8.1	8.5	7.9	0.19
Clinical score (geometric)	15.8	18.0	14.1	15.4	0.02

Values for age, height, weight, parasitaemia and clinical score are expressed as mean
*ANOVA test

Table 2: Association between nutritional status and clinical score, in accordance with history of malaria.

Correlation NS vs. CS	Primary episode (n = 47)		Previous episodes (n = 47)	
	rs	P value	*rs*	P value
General	-0.32	< 0.05	-0.19	0.20
Low parasitaemia	-0.49	< 0.01	-0.26	0.11
High parasitaemia	-0.08	0.77	0.18	0.62

NS = Nutritional Status; CS = Clinical Score

Wallis, and Spearman linear correlation tests were used for analysis of the variables, with 5% being adopted as the level of significance.

Results and Discussion

There was a predominance of males (71.3%, n = 67) in the group studied. The total average age was 34.9 ± 9.8 years. In all the individuals, the geometric mean parasitaemia ranged between 300 and 36,600 parasites/mm³, with an average of 6,946 ± 7,775 parasites/mm³ being recorded. Individuals from the eutrophic, overweight, and obese groups had similar parasitaemia in Ln (Kruskal Wallis test, $p > 0.05$) of 8.13 ± 0.97, 8.48 ± 1.25, and 7.90 ± 1.33 asexual forms of *P. vivax*/mm³, respectively. Significant difference was observed between mean clinical score in groups ($p = 0.02$) (Table 1).

Using Spearman linear correlation to analyze the relationship between the nutritional status and the clinical score of all the individuals, the correlation was shown to be negative (rs = -0.24, p = 0.02). In individuals with no history of malaria (first infection), in general this correlation is significantly and negatively stronger (rs = -0.32, p = 0.03). Using the same type of correlation, it was observed that among the individuals with low parasitaemia, there was a significant negative correlation between the nutritional status and the clinical score (rs = -0.37, p = 0.002). This information becomes more evident among individuals infected for the first time, for whom the value is highly significant (rs = -0.49, $p < 0.001$) (Table 2).

Currently, the adipose tissue as an endocrine organ is a production site for a number of cytokines and other bioactive substances. The expression of proinflammatory cytokines is proportional to the increase in BMI [4], which has an influence on the immune response of different groups of patients who are normal weight, overweight, or obese. There is a linear relationship between the increase in TNF-α levels and the severity of malaria [5].

However, obesity was a protective factor for the development of the cerebral form of *P. berghei* ANKA malaria in mice [6]. Moreover, considering the preliminary data from this study, it was found that individuals who were nutritionally classified as overweight and obese had a lower clinical score, which suggests a possible immunopathological link between obesity and the inflammatory response in infection by *P. vivax*. Thus, there is a need for further studies to better understand the physiopathological mechanisms of different nutritional profiles, especially obesity, in the clinical evolution of malaria.

Conclusion

Considering the multiple factors that interact with the severity of clinical expression of Malaria, this series cases seems to represent a protective factor between the overweight and obesity and clinical manifestations of malaria by *P. vivax* with low parasitemia in infected patients first. Whenever it is possible, it shall be performed a nutritional profile to all malaria patients. Other studies involving a controlled design to clarify this relationship will be needed.

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