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THE MALARIAL IMPACT ON THE NUTRITIONAL STATUS OF AMAZONIAN ADULT SUBJECTS

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SUMMARY

The anthropometric (body weight, height, upper arm circumference, triceps and subescapular skinfolds; Quetelet index and arm muscle circunference) and blood biochemistry (proteins and lipids) parameters were evaluated in 93 males and 27 females, 17-72 years old voluntaries living in the malarial endemic area of Humaita city (southwest Amazon). According to their malarial history they were assembled in four different groups: G1-controls without malarial history (n:30); G2 - controls with malarial history but without actual manifestation of the disease (n:40); G3 - patients with *Plasmodium vivax* (n:19) and G4 - patients with *Plasmodium falciparum* (n:31). The malarial status was stablished by clinical and laboratory findings. The overall data of anthropometry and blood biochemistry discriminated the groups differently. The anthropometric data were low sensitive and contrasted only the two extremes (G1>G4) whereas the biochemistry differentiated two big groups, the healthy (G1+G2) and the patients (G3+G4). The nutritional status of the *P. falciparum* patients was highly depressed for most of the studied indices but none was sensitive enough to differentiate this group from the *P. vivax* group (G3). On the other hand the two healthy groups could be differentiated through the levels of ceruloplasmin (G1<G2) and alpha nitrogen (G1>G2). Thus it seems that the malaria-malnourishment state exists and the results could be framed either as a consequence of nutrient sink and/or the infection stress both motivated by the parasite.

KEYWORDS: Malaria; Nutritional assessment; Malarial-malnourishment.

INTRODUCTION

Worldwide malaria is still the most important parasitic disease, viewed either from economic losses or damage to human health [25]. The disease is endemic in the Amazon accomplishing 96% of the 400,000 cases registered in the whole country in 1985 [12]. The city of Humaita (AM) showed 1,055 notified cases in 1984, being so included among the seven major endemic cities of the Brazilian state of Amazon.

Many are the factors involved in the interaction between the host and the parasite and one of the most important is the nutritional status of the host.

The interactions between malnutrition and infection are complex but are almost always synergistically deleterious to health. Both constitute the major public-health problem in underdeveloped regions lacking basic sanitation and populated by poor and iliterated people [2, 3, 4], and those characteristics are often found among the Humaita citizens.

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In much of developing world (such as Brazil) protein-energy malnutrition and malaria coexist at high prevalence, and one might expect to find enhancement of malarial infections a well-documented feature of protein-energy malnutrition.

Apart from the efforts of few studies [16, 17], information linking nutritional status and malaria in humans derives essentially from epidemiology observations.

Malaria possesses considerable potential for influencing adversely host nutrition. Malaria can restrict food intake through anorexia and vomiting. In its febrile phase it induces hipercatabolism with negative nitrogen balance and through its immunosupressive effects it may enhance susceptibility to infection with other pathogens with consequent further nutritional deterioration [2, 16]. Moreover malaria as a stressor can accentuate any marginal-nutritional deficiency either single of multiple. The malarial parasites are capable of synthesizing a very restricted number of aminoacids from glucose. Therefore, the principal sources of aminoacids for the intracellular parasite must be the free aminoacids of the red cell and the plasma, and the haemoglobin of the erythrocytes. On the other hand both erythrocytes and the parasites lack the enzymatic machinery for de novo synthesis of fatty acids, cholesterol, and phospholipids. Consequently both of these cells rely on passive exchanges with the blood plasma for these critical materials [9].

During the malarial infection those substances that serve either as macromolecular building blocks (aminoacids, nucleosides, fatty acids) or as energy sources (glucose) are transported into the infected cell at accelerated rate when compared to the uninfected cell and this enhanced entry is related to the developmental stage of the intracellular parasite [24]. Due to the membrane leaking there is a downhill movement of substances into the parasitized red cell allowing the parasite to have access to a wider array of substances than that of the uninfected red cell, so that the parasite acts as a metabolic sink [24].

It seems that malaric patients might have higher nutritional requirements mainly due to the parasite sink and infection stress in association with lower intake (anorexia) and lower availability (vomiting and either helminthic infestations or bacterial infections) of food. Thus the patient malnutrition might be cause in the as much as consequence of the malaric state. In the present study nutritional parameters were assessed in patients with *Plasmodium falciparum* and *Plasmodium vivax* malaria and the results compared with those found for healthy individuals who had or had not prior history of malaria attacks, all living in the same endemic area.

SUBJECTS AND METHODS

Subjects

The study envolved 120 individuals, 93 males and 27 females, 17-72 years old voluntaries living in the malarial-endemic area of the Brazilian southwest Amazon (Humaita city). The individuals were classified according to their malarial history in four groups: G1 - Healthy controls without malarial history (n=30), G2 - Healthy subjects with malarial history (n=40), G3 - *Plasmodium vivax* malarial patients (n=19), G4 - *Plasmodium falciparum* malarial patients (n=31).

Methods

The malarial diagnosis was done individually by the thick-smear technic of the peripheral blood which was used for parasite countings [5].

The measurement of body weight and height were obtained in an anthropometric 0.1 kg and 0.5 cm precision scale. The results were used for the Quetelet index calculation [8, 10]. Upper arm circumference (AC) and triceps skinfold (TSF) were measured at the midpoint of the nondominant arm according to standard methods using an insertion tape and a Lange caliper. Arm muscle circumference (AMC) was calculated from the expression AMC = AC - (3,14 x TSF) [7].

Antecubital-vein blood was drawn from each individual after a 10-12 hour fasting period. The EDTA-blood was saved under refrigeration for hematimetric measurements. The decanted serum was splited and the aliquots stored frozen for further biochemical analysis except for glucose, urea-N and bilirrubins that were assayed at the same day. Hematocrits were measured after blood centrifugation in micro-hematocrit tubes. Hemoglobin was determined by the cyanmethemoglobin method [20]. Serum total protein was measured using the biuret reaction [20], albumin and globulins fractions were calculated after serum-protein electrophoresis in agarose-gel [20]. Transferrin and ceruloplasmin were measured by the radial immunodiffusion technique [11]. Total lipids, cholesterol, triglycerides and alpha-amino nitrogen were assayed colorimetrically [20] and free-tryptophan fluorimetrically [26].

A fresh-stool sample was taken from each subject and used for helminthic detection [20].

The Statistical analysis of the four groups included: the discriminatory analysis of each variable showing its discriminatory capacity and the x^2 test for the stool-worm comparisons [1].

RESULTS

The groups were statistically homogeneous for the variables age, blood glucose and urea and partially uniform for the sex due to the lower number of female on group IV (Table 1).

Both patient groups were similar for the findings: hepatic and spleenmegaly (frequency and lenght) positive parasitemia, fever and diarrhea at the moment of the clinical examination and all showed hematimetric alterations (Table 1).

The *P. falciparum* malarial patients (group IV) were characterized by their higher intensity of parasitemia, severe anemia and higher vomiting frequency whereas the *P. vivax* patients showed higher levels of bilirrubin and higher helminthic parasitosis (Table 1).

The anthropometric measurements as a whole were able to differentiate only the groups G1 and G4, with the highest discrimination power being showed by the body weight, upper arm circumference and subescapular skinfold parameters (Table 2). On the other hand the overall nutritional-biochemistry results distinguished the two major groups, the healthy (G1+G2) and the patients (G3+G4) with all but one (gamma globulin) parameter showing high discriminating power (Table 3).

The nutritional status of the *P. falciparum* patients was highly depressed as shown by mostly of the studied tests however none was sensitive enough to differentiate this group from the *P. vivax* one (G3). On the other hand the two healthy groups (G1 and G2) were able to be distinguished one from the other through the levels of ceruloplasmin (G1<G2) and alpha amino nitrogen (G1>G2).

TABLE 1

Sex, age and general laboratory features of the groups of subjects

Variables			Groups [1]				Statistic Interpretation
			G1	G2	G3	G4	
Sex and age	Males		26	32	11	28	x^2=8.93 (P<0.05)
	Females		4	8	8	8	(G1=G2=G4) > G3 for males
	17-30 YRS		14	15	11	11	x^2=3.09 (P > 0.30)
	>30 YRS		16	25	8	20	G=G2=G3=G4
Hematimetry	Globular volum		51 ± 3.9	47 ± 8.3	41 ± 6.1	40 ± 5.5	(G1=G2) > (G3=G4)
	Hemoglobin	(g/dl)	14.9 ± 1.8	14.9 ± 2.8	13.2 ± 1.9	12.0 ± 2.3	(G1=G2) > G4
	Hematocrit	(%)	50 ± 3.9	49 ± 7.2	41 ± 53	39 ± 5.3	(G1=G2) > (G3=G4)
	HSR	(mm/h)	6.5 ± 4.8	17 ± 19	35 ± 14	38 ± 14	G1 < G2 < (G3=G4)
	Total leukocytes	(/mm³)	5.579 ± 1.195	5.368 ± 1.622	4.400 ± 1.716	4.761 ± 1.329	(G1=G2) > (G3=G4)
	Bast.	(%)	0.24 ± 0.51	0.66 ± 0.78	2.18 ± 1.74	3.61 ± 8.52	(G1=G2) < (G3=G4)
	Neutrophil	(%)	46 ± 16	47 ± 9	45 ± 9	54 ± 15	(G1=G2=G3) < G4
	Eosinophil	(%)	6.6 ± 4.8	9.5 ± 7.4	5.1 ± 4.6	4.3 ± 4.0	G2 > (G3=G4)
	Lymphocytes	(%)	41 ± 15	37 ± 8	41 ± 8	33 ± 15	G1=G2=G3=G4
	Monocytes	(%)	6.6 ± 3.6	5.3 ± 2.3	7.6 ± 3.3	5.7 ± 3.1	G2 < G3
Plasma Chemistry	Glucose	(mg/dl)	104 ± 15	105 ± 12	113 ± 16	106 ± 22	G1=G2=G3=G4
	Urea	(mg/dl)	27 ± 7.5	28 ± 8.2	29 ± 13	31 ± 15	G1=G2=G3=G4
	Total bilirrubin	(mg/dl)	0.60 ± 0.23	0.52 ± 0.21	0.91 ± 0.76	0.56 ± 0.23	(G1=G2=G4) < G3
Fecal Parasitosis	negative		19	21	4	10	(G1=G2) > (G3=G4)
	Monoparasite		7	10	6	14	(G1=G2=G3) < G4
	Polyparasite		4	9	9	7	(G1=G2=G4) < G3
	Ancylostomidae		7	10	12	13	(G1=G2) < (G3=G4)
	T. trichiuri		3	8	6	2	(G1=G2=G4) < G3

[1]Groups: G1 = Healthy controls without malarial history; G2 = Healthy subjects with malarial history; G3 = *Plasmodium vivax* malarial patients; G4 = *Plasmodium falciparum* malarial patients

TABLE 2

Anthropometric values of the groups of subjects.

Variables[1]		Groups[1]				Statistic Interpretation
		G1	G2	G3	G4	
Body Weight	(KG)	66.3 ± 10.8	63.5 ± 8.9	62.4 ± 12.8	57.6 ± 9.0	G1>G4
Height	(M)	1.65 ± 0.06	1.63 ± 0.06	1.63 ± 0.08	1.63 ± 0.08	G1=G2=G3=G4
Quetelet index	(KG/m^2)	24.2 ± 3.1	23.8 ± 2.5	23.3 ± 4.9	21.5 ± 2.6	(G1=G2=G3) > G4
TSF	(mm)	13.6 ± 5.0	13.7 ± 4.8	13.5 ± 5.7	11.3 ± 3.9	G1=G2=G3=G4
SESF	(mm)	16.8 ± 4.8	15.1 ± 3.9	14.6 ± 5.7	12.5 ± 3.4	G1>G4
Arm muscle Circumference	(mm)	241 ± 26	229 ± 42	232 ± 34	221 ± 22	G1=G2=G3=G4
Arm Circumference	(mm)	284 ± 35	275 ± 28	274 ± 43	256 ± 24	G1>G4

[1]Groups: G1 = Healthy controls without malarial history; G2 = Healthy subjects with malarial history; G3 = *Plasmodium vivax* malarial patients; G4 = *Plasmodium falciparum* malarial patients

TABLE 3

Serum proteins and lipids of the groups of subjeots

Variables[1]		Groups[1]				Statistic Interpretation
		G1	G2	G3	G4	
Total protein	(g/dl)	7.2 ± 0.6	7.2 ± 0.7	6.8 ± 0.7	6.6 ± 0.9	(G1=G2) > (G3=G4)
Albumin	(g/dl)	4.4 ± 0.6	4.1 ± 0.6	3.8 ± 0.5	3.5 ± 0.6	(G1=G2) > (G3=G4)
α 1-Globulin	(g/dl)	0.25 ± 0.06	0.27 ± 0.08	0.31 ± 0.09	0.33 ± 0.08	(G1=G2) < G4
α 2-Globulin	(g/dl)	0.43 ± 0.12	0.48 ± 0.13	0.39 ± 0.16	0.39 ± 0.12	G2 > (G3=G4)
β - Globulin	(g/dl)	0.70 ± 0.16	0.71 ± 0.14	0.61 ± 0.14	0.60 ± 0.18	(G1=G2) > (G3=G4)
δ - Globulin	(g/dl)	1.46 ± 0.33	1.64 ± 0.53	1.75 ± 0.47	1.71 ± 0.51	G1=G2=G3=G4
Transferrin	(mg/dl)	279 ± 42	259 ± 35	225 ± 51	200 ± 46	(G1=G2) > (G3=G4)
Ceruloplasmin	(mg/dl)	36 ± 9.5	51 ± 17	54 ± 17	54 ± 16	G1 < (G2=G3=G4)
α - Nitrogen	(mg/dl)	7.4 ± 1.0	6.8 ± 0.8	6.5 ± 0.7	6.6 ± 1.2	G1 > (G2=G3=G4)
Free tryptophan	(ug/ml)	16 ± 4.8	14 ± 4.8	11 ± 4.7	12 ± 5.9	(G1=G2) > G3
Total lipids	(mg/dl)	502 ± 148	480 ± 140	395 ± 178	383 ± 96	(G1=G2) > (G3=G4)
Cholesterol	(mg/dl)	271 ± 63	273 ± 55	200 ± 61	203 ± 63	(G1=G2) > (G3=G4)
Triglycerides	(mg/dl)	108 ± 57	107 ± 55	137 ± 52	150 ± 61	(G1=G2) < G4

[1]Groups: G1 = Healthy controls without malarial history; G2 = Healthy Subjects with malarial history; G3 = *Plasmodium vivax* malarial patients; G4 = *Plasmodium falciparum* malarial patients

Among the biochemical parameters the malarial patients were characterized by their reduced levels of total protein, albumin, beta-globulin, transferrin, alpha-amino nitrogen, tryptophan, total lipids and cholesterol along with their increased levels of ceruloplasmin and triglycerides (Table 3).

DISCUSSION

The four groups of individuals were assembled based on their classical malarial findings of history, clinics and laboratory [19].

The *P. falciparum* malarial patients showed the highest incidence of anorexia, vomiting and intensity of parasitaemia. This form of the disease is usually referred as the most severe of the two forms of malaria studied [18]. This group presented the worse nutritional status according to most of the studied indices. The decreasing of food availability by anorexia, vomiting, diarrhoea and helmintic parasitosis in association with the sinking of nutrients by the parasite and the infection hipercatabolic state could account for shortaging the body energy stores mainly adipose tissue and skeletal muscle as indicated by the lower body weight and other anthropometric measurements. In the same way one could concern about the contribution of their higher water lost rate due to factors such as fever-sweating,

diarrhea and vomiting all common features of this group of patients.

The serum protein pattern of the malarial patients showed decreased levels of the nutritional sensitive proteins such as albumin, beta-globulin and transferrin and an increased level of the acute-phase reactant proteins such as the alpha 1-globulin group and ceruloplasmin paralelling the lower circulating aminoacids (alpha-amino nitrogen) and tryptophan. These changes in the pattern of liver protein synthesis is a general feature of the infection state [2]. In this condition usually the reduced plasma concentration of most free-aminoacids results from their egress from plasma caused by an accelerate uptake by hepatic parenchymal cells. Concomitantly skeletal muscle, skin and other tissues display a net loss of their protein content. Degraded body proteins thereby contribute importantly to the free amino acids enter the liver through the plasma and return as various acute-phase reactant glycoproteins (alpha-1-globulin) promptly secreted back to the plasma [2]. This metabolic adaptation is important for the host defense by contributing to the effectiveness of phagocytic activity, the development of organism-specific immunity and repair of tissue damage [21].

The changes in serum total lipids, cholesterol and phospholipids during malaria varied depending on the experimental model which has been used [14]. In our case the cholesterol and total lipid levels were significantly lower in the malarial patients. The reported fall in serum cholesterol could be postulated as consequent to either or both the impaired hepatic function for its synthesis and esterification or/and increased uptake of cholesterol by the infected erythrocytes [6, 23, 24].

The increased triglycerides levels found in sera of malarial patients are usually unespecific to the Plasmodium strain and more likely related to the parasitaemia grade as well the hepatomegaly [14]. It seems that two independent mechanisms one pre-and another post-hepatic could respond for the high levels of triacylglyceride in malaria. The pre-hepatic event begins with the increase in non-esterefied fatty acids (NEFA) in the plasma of infected host which indicates that peripheral adipose tissue lipids are being degraded, mobilized and transported to the liver [6]. It seems that the parasite itself could be able to induce this peripheral lipolysis in order to meet its own needs for fatty acids with the excess being taken up by the liver [15]. Moreover anorexia as well the infection stress could promote hyperactivity of the sympathetic nervous system and a catecholamine stimulated mobilization of NEFA from adipose tissues [6]. This increased inflow of NEFA to the liver would promote higher hepatic synthesis and secretion of tricylglycerides rich lipoproteins as seen in malarial-infected plasma [6, 13, 15]. The higher circulating triglycerides might manifest itself as a post-hepatic event and can be maintained by the lower lipid clearance due to a reduced activity of the lipoprotein lipase (LLP) [6, 13]. Is has been suggested also that the systemic reduction of the LLP activity could be consequent to the action of the Tumor Necrosis Factor (TNF) a cytokine found increased in sera from malarial patients [22].

RESUMO

Impacto da malaria no estado nutricional de doentes adultos da Amazônia

A avaliação antropométrica (pêso, altura, circunferência branquial, prega cutânea tricipital, prega cutânea subescapular, índice de Quetelet e circunferência muscular do braço) e bioquímica (proteínas e lipides) foi realizado em 120 indivíduos (93 masculinos e 27 do sexo feminino), de 17 a 72 anos de idade, moradores de área endêmica de malária (Humaitá - AM). De acordo com a história da doença (malária) eles foram divididos em 4 grupos: G1 - controle (n = 30), sem história de malária; G2 - controle (n = 40), com história de malária, mas sem manifestação de doença atual; G3 - doentes com *Plasmodium vivax* (n = 19) e G4 - doentes com *Plasmodium falciparum* (n = 31). O diagnóstico de malária foi estabelecido por manifestações clínicas e confirmado laboratorialmente (gota espessa e esfregaço). No global as medidas antropométricas e bioquímicas discriminaram os grupos diferentemente. As medidas antropométricas do pêso, altura, reservas calóricas e estoque proteicos somáticos, apresentaram pouca sensibilidade, discriminado apenas os grupos extremos (G1 > G4). As medidas bioquímicas, no geral diferenciaram dois grandes grupos, os sadios e os doentes (G1+G2) e (G3+G4). Os doentes com *Plasmodium falciparum* (G4) foram os que se apresentaram em pior estado nutricional para a maioria das variáveis, sem entretanto, nenhuma variável individual que os discriminasse significativamente do G3. Estes dados permitem concluir que a malária resulta em desnutrição do hospedeiro, cuja gravidade está relacionada ao tipo e estágio da doença.

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