Rev. Inst. Med. trop. São Paulo
37 (6): 493-500, novembro/dezembro, 1995.

EFFECT OF SKIN COLOUR AND SELECTED PHYSICAL CHARACTERISTICS ON *SCHISTOSOMA MANSONI* DEPENDENT MORBIDITY

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SUMMARY

The effect of the colour group on the morbidity due to *Schistosoma mansoni* was examined in two endemic areas situated in the State of Minas Gerais, Brazil. Of the 2773 eligible inhabitants, 1971 (71.1%) participated in the study: 545 (27.6%) were classified as white, 719 (36.5%) as intermediate and 707 (35.9%) as black. For each colour group, signs and symptoms of individuals who eliminated *S.mansoni* eggs (cases) were compared to those who did not present eggs in the faeces (controls). The odds ratios were adjusted by age, gender, previous treatment for schistosomiasis, endemic area and quality of the household. There was no evidence of a modifier effect of colour on diarrhea, bloody faeces or abdominal pain. A modifier effect of colour on hepatomegaly was evident among those heaviest infected (≥ 400 epg): the adjusted odds ratios for palpable liver at the middle clavicular and the middle sternal lines were smaller among blacks (5.4 and 6.5, respectively) and higher among whites (10.6 and 12.9) and intermediates (10.4 and 10.1, respectively). These results point out the existence of some degree of protection against hepatomegaly among blacks heaviest infected in the studied areas.

KEYWORDS: Schistosomiasis mansoni; Colour; Morbidity.

INTRODUCTION

Individuals chronically infected with *S.mansoni* range from asymptomatic to severe cases, characterized by hepatomegaly and portal hypertension. Some gastrointestinal complaints, such as diarrhea, abdominal pain and/or bloody faeces, have also been attributed to *S. mansoni* infection, but the most consistent finding has been the association between infection and bloody faeces [7, 15, 17, 20, 24].

There is strong evidence that the morbidity due to *S.mansoni* depends in part on the intensity of infection [28]. Other observations in Africa, St Lucia and Brazil have suggested that a further contributing factor is the "racial" admixture of infected individuals, with black people having some degree of protection against the development of splenomegaly due to *S.mansoni* infection [2, 8, 9, 16, 19]. Recent investigations have yielded results consistent with this view. A study undertaken in an endemic area of Brazil found splenomegaly to be less frequent in blacks as compared to white individuals,

This project was sponsored by UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Disease, by Financiadora de Estudos e Projetos (FINEP) and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq).

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even when the study participants were subjected to socioeconomic stratification [26]. Likewise, a separate study reported the existence of a protective effect of non-white subjects against enlargement of liver and bloody faeces; this effect persisted even after stratification for *S.mansoni* egg counts [21]. Possible reasons for these racial differences have been suggested. The most common explanation is related with the African origin of *S.mansoni*. Ancestral experience with infection may affect the immunological response and may account for lower morbidity among blacks [8]. More recently, factors affecting fibrogenesis that may be genetically determined have been identified. WYLER [29] postulated that the unmodified production of these fibrogenic signals may be responsible for schistosomiasis severe fibrosis; the contribution of the above mentioned factors to schistosomiasis morbidity in different racial groups is still unknown.

We here present the results of a study carried out in two endemic areas for schistosomiasis mansoni, aiming at examining the effect of colour group on bloody faeces, diarrhea, abdominal pain, liver and spleen enlargement, using quantitative measurements of skin colour and physical characteristics, and controlling the effects as completely as possible for confounding variables.

MATERIALS AND METHODS

Study areas and population

The study was undertaken in two endemic areas. The first (Comercinho) is a small town situated in the northeast of Minas Gerais state (rural zone). The second area (Gorduras) is a district of Belo Horizonte, the state capital, which is a city with around 2 million inhabitants (urban zone). Malaria and visceral leishmaniasis were not known to be endemic in the two studied areas.

The study areas were entirely mapped, natural water sources identified and all dwellings numbered in 1992. In Comercinho, a total of 1,850 resident individuals were identified through a census performed in all houses existing in the town. In Gorduras, a total of 1896 dwellings were identified, and the number of residents was estimated at around 9500 inhabitants (5 inhabitants per house).

Faecal examination

All eligible individuals received a container, labeled with name and study number, for collection of faeces. Two slides were prepared from each faecal sample and examined for the presence and number of *S.mansoni* eggs [10]. The number of eggs per gramme was estimated from the mean of the two slides examined.

In Comercinho, all residents were eligible for faecal examination. In Gorduras, a simple random sample of 650 households was selected and 3290 individuals were identified; all residents in the sampled households were eligible for stool examination. Assumptions for the sample size calculation were the following: number of inhabitants = 9480 (5 per dwelling); prevalence of *S.mansoni* infection = 0.20; precision = 0.20; type 1 error = 0.05; correction for design effect = 2; loses = 0.20 [4, 27].

Clinical examination

Clinical examination was undertaken in both areas by a single physician without prior knowledge of the results of the faecal diagnosis or colour classification. The examination was undertaken with the patients lying on their back and in the right lateral position. The liver was considered palpable when detectable immediately under the costal margin with the breath held.

All patients were submitted to a questionnaire concerning the occurrence of diarrhea, abdominal pain or bloody faeces in the preceding 30 days as well as previous history of treatment for schistosomiasis and splenectomy.

Quality of the household

The quality of the household was adopted in this study as an indicator for the socioeconomic-economic level of the family. This information was obtained by direct observation of the materials used for construction. Selected materials were scored and the sum of these determined the quality of the dwelling, as previously described [13].

Colour classification

Determination of colour group was undertaken by a single team member without knowledge of infection status or clinical examination results. Classification was made by comparison with standard photographs and based on skin pigmentation, eye colour, hair texture and shape of nose and lips. The physical characteristics were scored as follows: hair (smooth hair = 6, wavy = 4, curly = 2 and frizzy = 0); nose (thin nose = 4, intermediate = 2 and Negroid = 0); lips (thin = 4, intermediate = 2 and Negroid = 0); eyes (blue, green, yellow or light brown eyes = 2, dark brown or black

eyes = 1). Skin pigmentation was estimated by color reflectometry using the inner arm with the apparatus at a distance of 9 cm. This anatomical site was selected since it is accessible but not exposed to direct sunlight [11, 12]. Measurement were made under rigidly controlled physical conditions and luminosity (1,000 watt halogen lamp in an otherwise dark room) using a LunaPro photometer which was standardized before each work session. The measurement ranged from 15.33 to 19.67 and were scored as follows: 15.00 to 15.99 = 0, 16.00 to 16.99 = 2, 17.00 to 17.99 = 3, 18.00 to 18.99 = 5, 19.00 to 20.00 = 6. Final classification was into one of three groups: Whites (total > 13), Intermediates (total between 10 and 13) and Blacks (total < 10).

Study design

In Comercinho, all individuals > 2 years of age living in the town in the year of 1992 were eligible for the present study (n = 1737). The resident individuals were examined by our team in 1974, 1981, 1983, 1988, 1990-92. During each of these years, faecal examinations were performed by the Kato-Katz method [10], the same pre-coded standard clinical form was used, and all clinical examinations were performed by the same physician. Since 1981, those who presented *S.mansoni* eggs in faeces were treated with oxamniquine. All individuals who received treatment before 1992 were identified. The age, infection status, egg counts, and clinical data considered were those of the last year before the individual's first treatment. In Gorduras, a simple random sample of individuals > 2 years of age who presented eggs in their faeces (518/609) and a simple random sample of those > 2 years of age who did not present *S.mansoni* eggs (518/2256) was selected. All information was obtained on cross sectional basis in 1992.

Cases were defined as those with *S.mansoni* eggs and controls were defined as those without eggs in the faecal examination.

Statistical analysis

Chi-square and Fisher's exact test were used to examine differences between proportions[1]. Multivariate analysis was based on multiple logistic regression [3]. Odds ratios for each sign or symptom were adjusted for age (2-9=1, 10-19=2 and ≥ 19 yrs=3), gender (male = 1, female = 2), previous treatment for schistosomiasis (no = 1, yes = 2), quality of the household (better = 1, worse = 2), and endemic area (Gorduras = 1, Comercinho = 2). The criteria for inclusion of socio-demographic variables in the logistic model was association with infection beyond 0.20 [6] level in at least one color group. The existence of an effect modifier between colour and intensity of infection on palpable liver at the middle clavicular and middle sternal lines was examined under the addictive and multiplicative models in the univariate analysis; interaction was also examined under the multiplicative model in the multiple logistic regression. The results obtained in the two endemic areas were pooled to again power for the statistical analysis. The analysis was carried out using the EGRET and the SAS (1988) software packages [22, 23].

RESULTS

Two thousand seven hundred and seventy three individuals were eligible for this investigation. Of these, 1971 (71.1%) participated in the study. Five hundred and forty five (27.6%) participants were classified as whites, 719 (36.5%) as intermediates and 707 (35.9) as blacks; there were no Asians or Brazilian Indians in the studied areas. Individuals classified as whites, intermediates and blacks presented the following characteristics: curly or frizzy hairs, 11.8, 51.7 and 100.0%; intermediate or Negroid nose, 30.1, 65.5 and 84.4%; intermediate or Negroid lips, 23.2, 57.5 and 80.2%; dark brown or black eyes, 39.8, 62.6 and 83.4; mean colour reflectometry, 17.987 (SD=0.621), 17.402 (SD=0.536) and 16.495 (SD=0.521), respectively.

Table 1 shows the associations of socio demographic variables and previous treatment with *S.mansoni* infection, according to the colour group. Age and study area were associated with infection ($p < 0.05$) among whites, intermediates and blacks. Previous treatment and gender were associated with infection among blacks ($p < 0.05$). Quality of the household was associated with infection among blacks at < 0.20 level.

Table 2 shows the results of the univariate analysis of selected signs and symptoms and *S.mansoni* infection, according to colour group. For white, intermediate and black colour groups, bloody faeces, diarrhea, palpable liver at the middle clavicular line and palpable liver at the middle sternal line were associated with infection ($p < 0.05$). Abdominal pain was associated with *S.mansoni* infection among whites and intermediates ($p < 0.05$). The percentages of cases with splenomegaly varied from 1.0 (blacks) to 2.2 (whites), while among controls they varied from 0.0 (intermedi-

TABLE 1

Univariate analysis of socio demographic variables, previous treatment and *S. mansoni* infection, according to the colour (white, intermediate and black)

Variables	*White*		*Intermediate*		*Black*	
	Cases (n=277) %	Controls (n=268) %	Cases (n=378) %	Controls (n=341) %	Cases (n=395) %	Controls (n=312) %
Age (Yrs)						
2-9	3.3	43.4	7.9	40.9	8.7	34.1
10-19	29.2	19.5	36.2	22.5	39.1	28.0
≥ 20	67.5	37.1	55.9	36.6	52.2	37.9
	p<001		p=000		p<001	
Gender						
Males	45.5	43.3	38.1	40.5	65.6	46.2
Females	54.5	56.7	61.9	59.5	34.4	53.8
	p=0.605		p=0.515		p=0.000	
Quality of the household						
Better	84.5	87.7	75.9	77.4	73.9	79.8
Worse	15.5	12.3	24.1	22.6	26.1	20.2
	p=0.280		p=0.637		p=0.067	
Area						
Gorduras	30.0	43.3	36.5	55.4	35.2	27.9
Comercinho	70.0	56.7	63.5	44.6	64.8	72.1
	p=0.001		p=0.000		p=0.039	
Previous treatment						
No	91.0	88.5	91.0	90.9	82.8	89.4
Yes	9.0	11.5	9.0	9.1	17.2	10.6
	p=0.329		p=0.964		p=0.012	

Cases: presence of *S. mansoni* eggs in stools; Controls: absence of *S. mansoni* eggs in stools; p = p value (chi-square test)

TABLE 2

Univariate analysis of selected signs and symptoms, previous treatment and *S. mansoni* infection, according to the colour group (white, intermediate and black)

Variables	*White*		*Intermediate*		*Black*	
	Cases (n=277) %	Controls (n=268) %	Cases (n=378) %	Controls (n=341) %	Cases (n=395) %	Controls (n=312) %
Abdominal pain						
No	63.6	77.4	53.4	65.5	64.1	68.9
Yes	36.4	22.6	46.6	34.5	35.9	31.1
	p=0.000		p=0.001		p=0.183	
Bloody faeces						
No	90.6	99.6	87.7	97.9	89.6	99.0
Yes	9.4	0.4	12.3	2.1	10.4	1.0
	p=0.000		p=0.000		p=0.000	
Diarrhea						
No	77.9	90.3	74.9	89.6	78.9	87.4
Yes	22.1	9.7	25.1	10.4	21.1	12.6
	p=0.000		p=0.000		p=0.004	
Palpable liver at middle clavicular line						
No	84.5	93.3	82.0	89.4	88.1	92.6
Yes	15.5	6.7	18.0	10.6	11.9	7.4
	p=0.001		p=0.005		p=0.044	
Palpable liver at middle sternal line						
No	83.1	93.7	83.3	90.9	88.3	93.3
Yes	16.9	6.3	16.7	9.1	11.7	6.7
	p=0.000		p=0.003		p=0.027	
Palpable spleen						
No	97.8	99.6	98.1	100.0	99.0	99.7
Yes	2.2	0.4	1.9	0.0	1.0	0.3
	p*=0.066		p*=0.010		p*=0.268	

Cases: presence of *S. mansoni* eggs in stools; Controls: absence of *S. mansoni* eggs in stools; p = p value (chi-square test); p* = p value (Fisher's Exact test)

TABLE 3

Results of the multivariate analysis of selected signs and symptoms and *S. mansoni* infection, according to the colour group (white, intermediate and black)

Signs/ symptoms	White OR (CI-95%)*	Intermediate OR (CI-95%)*	Black OR (CI-95%)*
Abdominal pain	1.4 (0.9-2.2)	1.6 (1.0-2.3)	1.3 (0.9-1.9)
Bloody faeces	9.9 (1.3-75.2)	8.9 (1.6-29.2)	9.2 (2.7-31.0)
Diarrhea	2.0 (1.1-3.8)	2.7 (1.6-4.6)	1.8 (1.1-2.8)
Palpable liver at middle clavicular line	5.5 (2.3-13.3)	2.3 (1.3-4.1)	2.4 (1.3-4.5)
Palpable liver at middle sternal line	7.0 (2.8-17.5)	2.0 (1.2-4.0)	2.2 (1.2-4.2)
Palpable spleen	5.7 (0.4-84.9)	-	1.6 (0.7-14.9)

OR = Odds ratio adjusted by multiple logistic regression method for age, gender, previous treatment, endemic area and quality of the household
CI-95% = Confidence interval at 95% level

ates) to 0.4 (whites); only for the black colour group was the difference between cases and controls significant.

Table 3 shows the results of the multivariate analysis of selected signs and symptoms and *S.mansoni* infection. The odds ratios were adjusted for age, gender, previous treatment, endemic area and quality of the household. Bloody faeces, diarrhea and palpable liver at the middle clavicular and middle sternal lines persisted associated with *S.mansoni* infection among whites, intermediates and blacks after the above mentioned adjustments. The odds ratios for bloody faeces and diarrhea were reasonably similar among whites, intermediates and blacks. The odds ratios for palpable liver at the middle clavicular line and at the middle sternal line were 2 to 3 times higher among whites than among intermediates and blacks (5.5 vs. 2.3 and 2.4; 7.0 vs. 2.0 and 2.2, respectively). Odds ratio for palpable spleen were higher among whites in relation to blacks (5.7 vs. 1.6), but the confidence intervals were too large.

Table 4 and Figure 1 show odds ratios for palpable liver at the middle clavicular line and palpable liver at the middle sternal line, according to the number of *S.mansoni* eggs among whites, intermediates and blacks. The following results were obtained in the univariate analysis: (1) crude odds ratios for palpable liver at the middle clavicular and at the middle sternal lines increased progressively with the increase of *S.mansoni* faecal egg counts (dose-response relationship); this was observed for all the colour groups; (2)

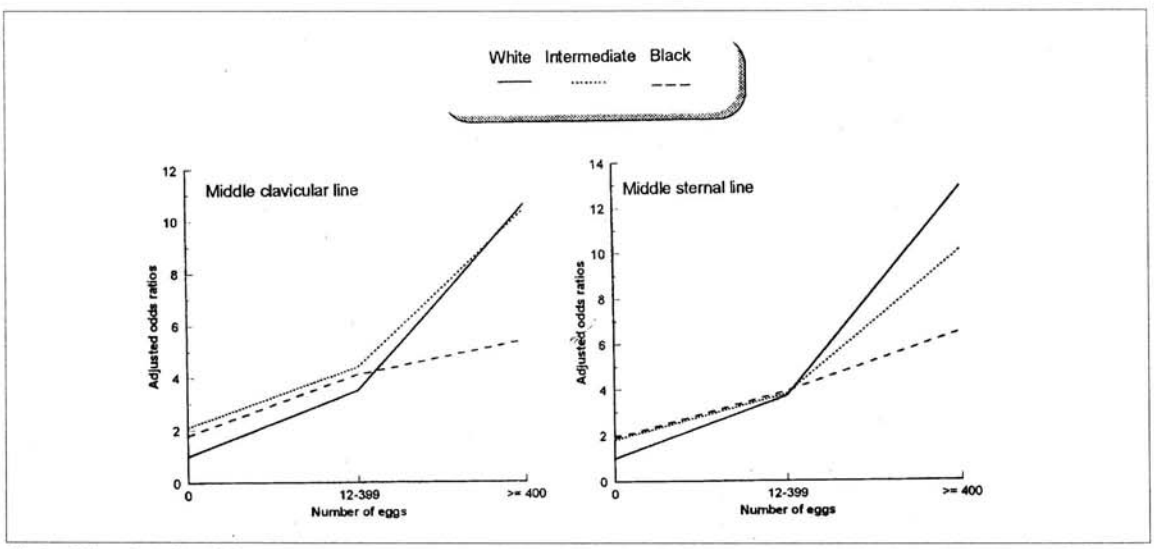

Fig. 1 - Odds ratios (adjusted for age, gender, previous treatment, endemic area and quality of household, allowing for interaction in the multiple logistic regression method) for palpable liver at the middle clavicular and at the middle sternal lines, according to colour and number of *S. mansoni* eggs in stool.

TABLE 4

Odds ratios for liver palpable at the middle clavicular line and at the middle sternal line, according to colour and number of *S. mansoni* eggs in stools

Colour	Number of eggs per gramme		
	0	12-399	> 400
	OR (CI-95%)	OR (CI-95%)	OR (CI-95%)
		Middle clavicular line	
Crude odds ratios			
White	1.0	1.8 (1.0-3.4)	5.2 (2.4-11.2)
Intermediate	1.6 (0.9-3.0)	2.4 (1.4-4.3)	5.8 (3.0-11.5)
Black	1.1 (0.6-2.1)	1.7 (0.9-3.1)	2.3 (1.1-5.0)
		p value on 9 df < 0.001	
Adjusted odds ratios*			
White	1.0	3.5 (1.7-7.3)	10.6 (4.7-24.0)
Intermediate	2.1 (1.0-3.9)	4.4 (2.3-8.5)	10.4 (4.8-22.3)
Black	1.8 (0.9-3.7)	4.1 (2.1-8.1)	5.4 (2.4-12.2)
		p value on 15 df < 0.001	
		Middle sternal line	
Crude odds ratios			
White	1.0	2.0 (1.1-3.8)	6.6 (3.1-14.0)
Intermediate	1.5 (0.8-2.7)	2.2 (1.2-4.0)	6.2 (3.1-12.3)
Black	1.1 (0.5-2.1)	1.6 (0.9-3.1)	3.0 (1.4-6.2)
		p value on 9 df < 0.001	
Adjusted odds ratios *			
White	1.0	3.7 (1.8-7.6)	12.9 (5.7-29.2)
Intermediate	1.8 (0.9-3.6)	3.8 (1.9-7.5)	10.1 (4.6-21.9)
Black	1.9 (0.9-3.9)	3.9 (1.9-8.0)	6.5 (2.9-14.8)
		p value on 15 df < 0.001	

* Odds ratios adjusted for age, gender, previous treatment, endemic area and quality of the household, allowing for interaction in the multiple logistic regression method

p value = Log likelihood ratio statistic

CI-95% = Confidence interval at 95% level

for those who eliminated 12-399 eggs per gramme of faeces, the odds ratios for palpable liver at the middle clavicular and at the middle sternal lines were reasonably similar among whites, intermediates and blacks; (3) among those heavily infected (≥ 400 epg), the odds ratios for palpable liver at the middle clavicular and at the middle sternal lines were higher among whites (5.2 and 6.6, respectively) and intermediates (5.8 and 6.2) than among blacks (2.3 and 3.0, respectively). After adjustment for confounders, the same tendencies persisted; an interaction between colour and heavy egg counts was observed for both palpable liver at the middle clavicular line and at the middle sternal line.

DISCUSSION

The previous findings of some degree of protection among blacks against the morbidity due to *S.mansoni* infection was partially confirmed in this study. Our results point out the existence of an modifier effect of colour group (black) on hepatomegaly among those heaviest infected. This conclusion is reinforced by the existence of a dose-response relationship in the effect.

In a previous study some degree of protection against hepatomegaly and bloody faeces among non-whites was found [21]. Our results did not confirm the observation regarding bloody faeces. Some degree of protection against splenomegaly among blacks has been found in different endemic areas in Brazil, St Lucia and Africa [2, 16, 19, 26]. The same tendency was observed in the present study, but the number of individuals with splenomegaly was to small to permit a conclusive inference.

Brazil represents one of the few areas of the world in which schistosomiasis is endemic and where there is an important racial mixture of individuals sharing common living space and habits. This facilitates studies on the effect of color on morbidity due to schistosomiasis. The Brazilian population, however, does not exhibit easily defined distinct racial groups due to extensive intermarriage. For this reason we did not adopt the term race in our study and all precautions were taken to avoid inaccuracies. Observations and measurements were undertaken by a single investigator who was unaware of infection and clinical status of the individuals, and the classification was based on both on quantitative

measurement of relative skin color and physical characteristics.

Regarding other methodological aspects, the control for potential confounders was as complete as possible, including age, gender, previous treatment, endemic area and an objective indicator of socioeconomic situation (quality of the household). Because treatment can reduce the morbidity due to schistosomiasis [5, 25], information concerning clinical signs and symptoms was obtained, whenever as possible, before the individual's treatment. When this information was not available the data were collected on cross sectional basis. Because colour does not change with time or age, it seems unlikely that such procedures would have produced biased estimates.

Studies undertaken in endemic areas in different countries have found a consistent association of bloody faeces and *S.mansoni* infection as well as a consistent association between intensity of infection and hepatomegaly. Associations of diarrhea or abdominal pain with infection were observed in some endemic areas but not in others [7, 14, 15, 17, 18, 20, 21, 24]. In the present study, bloody stools and diarrhea were associated with *S.mansoni* infection in all colour groups, and this association persisted after adjustments for confounders. An association between intensity of infection and hepatomegaly was also observed. The odds ratios for palpable liver at the middle clavicular and at the middle sternal lines increased with increasing *S.mansoni* egg counts in whites, intermediates and blacks.

In sum, our results lead to the following conclusions: a) there was no evidence of a modifier effect of colour on diarrhea, bloody faeces or abdomial pain in the study population; b) a tendency for a protective effect among blacks against the presence of splenomegaly was observed, but the results are not conclusive due to insufficient power for analysis; c) due to as yet unknown mechanisms, the modifier effect of color group (black) against hepatomegaly among those heaviest infected was evident in the present study.

RESUMO

Efeito da cor da pele e certas características físicas na morbidade dependente de *Schistosoma mansoni*.

O efeito da cor na morbidade associada ao *Schistosoma mansoni* foi estudado em duas áreas endêmicas situadas no Estado de Minas Gerais, Brasil. Dos 2773 habitantes elegíveis, 1971 (71,1%) participaram do estudo: 545 (27,6%) foram classificados como brancos, 719 (36,5%) como intermediários e 707 (35,9%) como negros. Os sinais e sintomas dos indivíduos que eliminavam ovos de *S. mansoni* nas fezes (casos) foram comparados aos daqueles que não apresentavam ovos do parasita neste exame (controles). As razões de chance foram ajustadas por idade, gênero, tratamento anterior para a esquistossomose, área endêmica e qualidade do domicílio. Não houve evidência de um efeito modificador da cor para a ocorrência de diarréia, sangue nas fezes ou dor abdominal. Um efeito modificador da cor foi evidente entre aqueles com maiores contagens de ovos nas fezes (≥400 opg), no que se refere à hepatomegalia: as razões de chances foram menores entre indivíduos classificados como negros (5,4 e 6,5 para presença de fígado palpável nas linhas hemiclavicular e médio esternal, respectivamente) e maiores entre aqueles classificados como brancos (10,6 e 12,9, respectivamente) e intermediários (10,4 e 10,1, respectivamente). Estes resultados apontam para a existência de algum grau de proteção em relação à hepatomegalia entre indivíduos classificados como negros nas áreas endêmicas estudadas.

ACKNOWLEDGEMENT

The authors would like to thank Dr. Andrew Simpsom for the critical review of the manuscript and Dr. Naftale Katz for his support throughout this project.

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Recebido para publicação em 06/11/1995.
Aceito para publicação em 30/11/1995.