SHORT REPORT: HOOKWORM INFECTION IS ASSOCIATED WITH DECREASED BODY TEMPERATURE DURING MILD *PLASMODIUM FALCIPARUM* MALARIA

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Abstract. Malaria's pyrogenic threshold seems to depend on factors such as age and transmission patterns. We studied the temperature at admission of 200 patients with mild malaria and observed that after adjusting for body mass index, the presence of other helminths, and other confounders, only hookworm-infected patients had lower fever at admission that those without hookworm infection (37.5 ± 0.9 and 38 ± 0.8, respectively; \( P < 0.001 \)). Thus, we suggest the age dependence of the pyrogenic threshold could have been confounded by the epidemiology of iron deficiency.

Knowing the true magnitude of malaria morbidity is an important preliminary goal to malaria control. In hyperendemic areas, as it is quite common to find subjects with *Plasmodium falciparum* parasitemia without fever; the definitions of a malaria attack often require parasitemia to rise above a certain threshold, which may vary according to transmission levels.\(^1\) Within a given transmission pattern, the pyrogenic threshold seems to be an age-dependent feature: young children seem to have a much higher threshold than adults. This was attributed to age-dependent differences in anti-tumor necrosis factor antibodies. In a recent study, we observed that patients with mild malaria who also had helminth infections had significantly lower body temperatures at admission.\(^2\) An immunological effect, malnutrition, and hookworm-related iron deficiency were possible causes.

We studied case records from a series of 200 patients hospitalized for mild *P. falciparum* malaria at the Hospital for Tropical Diseases, Bangkok, Thailand, between 1995 and 1997. Mild malaria was defined by presence of *P. falciparum* infection and absence of any of the severity criteria of the World Health Organization.\(^4\) Temperature was measured orally with mercury thermometers. Routine clinical, demographical, and biological data was recorded. All patients had a stool examination by simple smear technique. Statistical analysis was performed by Student's unpaired \( t \)-test and multiple linear regression.

The mean age of patients was 27 ± 10 years (range, 15–62 years). The mean oral temperature at admission was lower in hookworm-infected patients than in those without hookworm infection (37.5 ± 0.9°C and 38 ± 0.8°C, respectively; \( P < 0.001 \)) and in *Strongyloides*-infected patients than in those without *Strongyloides* (37.5 ± 0.7°C and 37.9 ± 0.9°C, respectively; \( P = 0.03 \)). For those with and without *Ascaris* and *Trichuris* infection, there was no significant difference (*Ascaris*, 37.7 ± 0.9°C and 37.9 ± 0.9°C, respectively; \( P = 0.25 \)); and *Trichuris*, 37.7 ± 0.9°C and 37.9 ± 0.9°C, respectively; \( P = 0.11 \)).

We controlled for the effect of other variables by forcing the following variables in a multiple linear regression model: parasitemia, mean corpuscular volume, body mass index (either as categorical variables or as continuous variables), and the presence of all helminths (*Ascaris*, *Trichuris*, hookworm, and *Strongyloides*), hemoglobin, duration of symptoms, age, sex, and ethnic group. After adjusting for all the above variables, we found that only hookworm-infected patients had a significant negative association with decreased body temperature (beta coefficient, \(-3.8\); \( r = -2.6, P = 0.009 \)). There was a negative correlation between hemoglobin and oral temperature at admission (\( P = 0.01 \)). When adjusting for all the above variables, age and body mass index were not associated with any significant difference in temperature at admission (\( P = 0.9 \) and \( P = 0.5 \), respectively). Infection with *Ascaris*, *Strongyloides*, and *Trichuris* were not associated with decreased temperature at admission (\( P = 0.6, P = 0.11 \), and \( P = 0.7 \), respectively).

We believe that the fact that only hookworm was associated with lower oral temperature at admission suggested that the effect was more likely to result from hookworm-related iron deficiency than helminth-related Th1/Th2 shifts or other nutritional mechanisms. The mean corpuscular volume may not have been a very sensitive reflection of the iron status because of frequent hemoglobinopathies in the area (5%). It is well known that iron deficiency may be associated with hypothermia,\(^5\) that iron supplementation in malaria-endemic areas may be associated with increased malaria morbidity,\(^6,7\) and that hookworms are a common cause of iron deficiency in their hosts. The above suggest that the age dependence of the pyrogenic threshold to malaria parasites\(^8,9\) could have resulted from confounding by the epidemiology of hookworm infection, iron deficiency (which is also linked to age), or both.\(^6\) Demonstrating this would require further studies, including direct measurements of iron reserves and stool examinations.

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