Transactions of the Royal Society of Tropical Medicine and Hygiene 106 (2012) 701–708

Contents lists available at SciVerse ScienceDirect

Transactions of the Royal Society of Tropical Medicine and Hygiene

journal homepage: http://www.elsevier.com/locate/trstmh

Paradoxical associations between soil-transmitted helminths and *Plasmodium falciparum* infection

Julián A. Fernández-Niño[a,*], Alvaro J. Idrovo[b], Zulma M. Cucunubá[c], Patricia Reyes-Harker[a], Ángela P. Guerra[c], Ligia I. Moncada[a], Myriam C. López[a], Sandra M. Barrera[c], Liliana J. Cortés[c], Mario Olivera[a], Rubén S. Nicholls[a,c]

[a] *Grupo de Infecciones y Salud en el Trópico, Unidad de Parasitología, Departamento de Salud Pública, Facultad de Medicina, Ciudad Universitaria, Universidad Nacional de Colombia, Bogotá D.C, Colombia*
[b] *Centro de Investigación en Sistemas de Salud, Instituto Nacional de Salud Pública de México, Cuernavaca, México*
[c] *Grupo de Bioquímica, Grupo de Parasitología, Instituto Nacional de Salud, Bogotá, Colombia*

ARTICLE INFO

Article history:
Received 7 December 2011
Received in revised form 19 July 2012
Accepted 19 July 2012
Available online 11 August 2012

Keywords:
Helminths
Hookworm
Malaria
Ascaris lumbricoides
Epidemiology
Colombia

ABSTRACT

Evidence on the comorbidity between soil-transmitted helminth infections and malaria is scarce and divergent. This study explored the interactions between soil-transmitted helminth infections and uncomplicated falciparum malaria in an endemic area of Colombia. A paired case-control study matched by sex, age and location in Tierralta, Cordoba, was done between January and September 2010. The incident cases were 68 patients with falciparum malaria and 178 asymptomatic controls. A questionnaire was used to gather information on sociodemographic variables. Additionally physical examinations were carried out, stool samples were analysed for intestinal parasites and blood samples for Ig E concentrations. We found associations between infection with hookworm (OR: 4.21; 95% CI: 1.68–11.31) and *Ascaris lumbricoides* (OR 0.43; 95% CI: 0.18–1.04) and the occurrence of falciparum malaria. The effects of soil-transmitted helminths on the occurrence of malaria were found to be paradoxical. While hookworm is a risk factor, *A. lumbricoides* has a protective effect. The findings suggest that, in addition to the comorbidity, the presence of common determinants of soil-transmitted helminth infections and malaria could also exist. While the biological mechanisms involved are not clear, public health policies aimed at the control of their common social and environmental determinants are suggested.

1. Introduction

Malaria is considered to be the world's most important tropical infection; the disease affects 243 million people annually, causing 900 000 deaths each year, and contributing approximately 30% of the burden of disease attributable to tropical diseases.[1] Soil-transmitted helminth (STH) infections are chronic intestinal infections that are widely distributed globally and considered to be among the neglected tropical diseases.[2,3]

Malaria and STH infection tend to occur in the same regions and affect the same individuals; they share the same risk factors (overlapping phenomena) and their effects on morbidity, especially among pregnant women and children, are well known.[4,5] In the late 1970s the existence of a direct cause and effect relationship between STH infections and the occurrence of malaria was suggested.[6] It was then proposed that STH infections could be a risk factor or a protecting factor for the development of malaria. These hypotheses have been explored many times in the

* Corresponding author. Tel.: +57 1 316 5000x15032; fax: +57 1 316 5000x15033.
E-mail address: juliandesires@gmail.com (J.A. Fernández-Niño).

0035-9203/$ – see front matter © 2012 Royal Society of Tropical Medicine and Hygiene. Published by Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.trstmh.2012.07.012

past 10 years,[7] being supported by contradictory immunological models with some experimental evidence in animal models; this is primarily based on the potential shift to a Th2-type immune response as a result of STH infection, which would reduce the Th1-type response against malaria.[8]

The results of studies on the association between STH infections and the incidence of malaria have not been consistent. Four analytical studies, two cohort studies, two cross-sectional studies, one ecological study and a randomised controlled clinical trial found STH infections, or infection with a particular STH species, to be a risk factor for malaria.[9–14] In contrast, an ecological study[6] and two randomised clinical trials found a protective relationship.[15,16] A recent cross-sectional study in pregnant women found that while *Ascaris lumbricoides* had a protective association, hookworm was positively associated with the occurrence of malaria.[17] A case-control study reported no association.[18]

Several authors have drawn attention to the methodological limitations of these investigations.[7,19] These limitations include temporal ambiguity, lack of information on specific explored parasites and the potential role of confounding. The importance of considering the places where the participants in these studies live (location bias) has also been emphasised, because the observed associations could be explained through the geographical distribution of parasites.[12,20]

The present study was explicitly designed to assess the association between STH infections and the occurrence of uncomplicated falciparum malaria, and to explore the possible interactions between parasites by controlling for potentially confounding variables and for location bias.

2. Materials and methods

2.1. Design and study site

A case-control study matched by sex, age (range: 5–15, 16–45 and 46–60 years) and neighbourhood of usual residence was conducted between January and September 2010 in Tierralta (Cordoba, Colombia). Tierralta is the municipality with the highest number of reported cases of malaria in Cordoba, which in turn is one of the three departments with the highest incidence in Colombia. In 2010, 6204 malaria cases were reported for Tierralta, of which 25.53% were caused by *Plasmodium falciparum*. The people of Tierralta make their living from agriculture and rearing livestock; serious problems in accessing healthcare services are further complicated by the presence and substantial influence of illegal armed groups and drug traffickers.

2.2. Recruitment and selection

Each participant included in the study met the following criteria: had lived for at least 1 year in a rural area of Tierralta; had not received anthelmintic drugs within the previous 3 months; was aged between 5 and 60 years old; was not pregnant. Cases were defined as patients with a diagnosis of uncomplicated *P. falciparum* malaria confirmed by a thick blood smear, detected as incident cases during the study period at the centre for malaria diagnosis in the urban area of the municipality. All the included cases lived in one of 11 of the 19 rural areas of the municipality. Eight rural areas were excluded because of problems of access and concern for the security of the fieldwork team.

Controls were defined as individuals who lived within 500 m of the residence of the case with whom they were paired. Controls were required not to have had a malaria infection within the previous 3 months, nor to have reported having fever in the previous 15 days. All controls were subjected to a blood smear to rule out asymptomatic malaria infection. The selection and recruitment of controls required visiting the house of each participant during the week of his or her inclusion in the study. While at a participant's house we identified neighbours who could qualify as controls, and in order to recruit controls walked in a clockwise direction from the participant's house. One to three controls per case were recruited, depending on the possible candidates' availability and willingness to participate.

To control for a possible location bias, controls were required not to have left their neighbourhood for more than 3 consecutive days in the previous 3 weeks. This condition was intended to increase the likelihood that each case would have controls who may have acquired malaria in the same place of recruitment,[20] and who therefore shared the same ecological transmission risk.

2.3. Data collection

Participants responded to a socioeconomic survey and their place of residence was observed to measure relevant covariates that could act as confounding variables, on the basis of a recent systematic review.[7] The questionnaires were administered and the observations made by a physician trained in data collection instruments. The instruments used were previously validated with 70 individuals of the region in a pilot study with a good reproducibility (kappa: 0.82; 95% CI: 0.45–0.98).

On the day after their recruitment, at their place of residence, all participants underwent a general physical examination (height, weight, blood pressure, heart rate, respiratory rate, temperature, cardiovascular and respiratory auscultation, abdominal palpation) and were asked to provide a stool sample. Stool samples were preserved in 10% formalin and shipped by air for analysis at the parasitological laboratory of the National University of Colombia School of Medicine in Bogota. All the faecal samples underwent direct examination and the Ritchie–Frick modified concentration technique for diagnosis of STH and protozoa.[21] The samples were analysed independently by two experienced observers who were unaware of the status as cases or controls of the study subjects. Disagreements were discussed between both observers; the interobserver final concordance was very good (kappa 0.86; 95% CI: 0.63–0.91).

The thick blood smears from cases and controls were read out at the study site by a certified microscopy