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Epidemiology of helminth infections and their relationship to clinical malaria in southwest Uganda

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Summary It has recently been suggested that helminth infections may adversely influence susceptibility to other infections, including malaria. To investigate this hypothesis in a sub-Saharan African setting, surveys of helminth infections were conducted in 2003 among individuals who had been under weekly active case detection for clinical malaria during the preceding 18 months in four villages in Kabale District, southwest Uganda. Overall, 47.3% of individuals had at least one intestinal nematode species infection: hookworm, *Ascaris lumbricoides* and *Trichuris trichiura* were detected in 32.1, 17.4 and 8.1% of individuals, respectively. We found evidence of significant household clustering of *A. lumbricoides*, *T. trichiura* and hookworm, and clustering of heavy infection of each species. The association between helminth infection and clinical malaria was investigated in two villages and no evidence for an association was observed between the presence of infection or heavy infection and risk of malaria.

1. Introduction

The overlapping distribution of infection with intestinal helminths and malaria results in a high rate of co-infection (Buck et al., 1978; Petney and Andrews, 1998). In laboratory studies there is evidence suggestive of both synergism and antagonism in nematode and protozoa infections (Cox, 2001), and this may have implications for the epidemiology of multiple parasite species in humans. It has been suggested that by inducing elevated Th2 cytokine production and thus down-regulating Th1 type

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immune responses, helminth infections may influence the susceptibility to other infections, including malaria (Nacher et al., 2002b). Early studies in extremely malnourished populations suggested that *Ascaris lumbricoides* led to a suppression of malaria (Murray et al., 1977); other work in Zaire shows a positive association between infection with *A. lumbricoides* and *Plasmodium falciparum* (Tshikuka et al., 1996). Recent epidemiological data have suggested that *A. lumbricoides* is associated with a dose-dependent protection from cerebral malaria (Nacher et al., 2000, 2002a) but that the incidence of *P. falciparum* malaria was increased in helminth-infected individuals (Nacher et al., 2002b). It has also been noted in Madagascar that the prevalence of acute malaria attacks decreased dramatically following anthelminthic treatment (Jambou et al., reported by Mutapi et al., 2000). Given the potential importance these findings have for future malaria vaccines (Nacher, 2001), and to rule out the possibility that socio-economic confounding and household clustering of infections explain some of the associations reported, further data from well-characterized populations in other transmission settings are needed.

In southwest Uganda, malaria transmission is low and unstable, such that the risk of disease is spread among all ages and occasional epidemics occur (Kilian et al., 1999; Lindblade et al., 1999). Intestinal nematodes, hookworm, *A. lumbricoides* and *Trichuris trichiura* are also prevalent but no transmission of schistosomiasis occurs in the area (N.B. Kabatereine et al., unpublished data). As part of ongoing investigations of the epidemiology of clinical malaria in Kabale District, southwest Uganda, we undertook a community survey of intestinal nematodes. We present here some of the basic epidemiological characteristics of helminths among community members, and investigate the hypothesis that helminths increase susceptibility to malaria by looking at the association between helminth infection and clinical malaria as detected through active surveillance.

2. Materials and methods

Fieldwork was carried out in four villages of Kamwezi sub-county, Kabale District: Rwandamira, Kikuto, Kabirizi and Kigara A (1°12′7″–1°15′19″S, 30°10′48″–30°13′25″E). The study area lies at an altitude of 1454–1688 m asl. The area has a mean average temperature of 18 °C, with occasional temperatures of 10 °C at night. The average rainfall is 1000–1480 mm with two peaks, March–June and September–December. Malaria transmission is low and unstable and usually occurs in periodic peaks, shortly after the peaks of rainfall (Kilian et al., 1999; Lindblade et al., 1999). Malaria is predominantly caused by *P. falciparum* (Lindblade et al., 1999; Ndyomugyenyi et al., 2004). Previous entomological research conducted in the area indicates that throughout the district, *Anopheles gambiae* s.l. (90% of captures) was the principal malaria vector (Lindblade et al., 1999, 2000).

As part of a study of malaria epidemiology, weekly active case detection was carried out from November 2001 until May 2003. Stool samples were collected from community members and household socio-economic surveys were undertaken in May 2003. Since November 2001, all households in every village have been visited weekly by health workers. Axillary temperature was measured with a digital thermometer and finger-prick blood samples were taken from household members reporting febrile illness in the previous 24 hours. Blood slides were stained and stored at the health centre before being transported to Kampala for inspection by an experienced microscopist at the Vector Control Division, Ministry of Health. Individuals with parasitaemia and fever of ≥37.5 °C, with no signs of other infection, were defined as cases. Due to the high volume of blood slide processing arising from weekly active malaria screening in the villages, identification of malaria parasites to species level was not possible; however, previous studies indicate that *P. falciparum* is predominantly responsibility for malaria in the area (Lindblade et al., 1999; Ndyomugyenyi et al., 2004). Cases were recorded and treated with sulfadoxine–pyrimethamine on the day of household visit. Due to frequent population movements in Kabirizi, and Kigara A, malaria data from Rwandamira and Kikuto only were considered in the analysis of the association of malaria and helminths.

In May 2003, households in the four study villages were invited to participate in the helminth survey. Faecal samples were collected from participating household members and duplicate slides were examined within 60 minutes using the Kato–Katz method. Crude egg counts were recorded and converted to eggs per gram (epg). The 90th percentile was used to define a heavy infection, rather than an absolute threshold epg for high intensity, since it has been demonstrated that *A. lumbricoides* fecundity varies geographically (Hall and Holland, 2000). A percentile threshold allows heavy infections to be defined in a community-specific manner when worm burden is measured indirectly by egg count. Individuals found to be positive for helminths were administered a single-dose treatment of albendazole.