Reviewer's report

Title: Human immunodeficiency virus infection is a risk factor for cerebral malaria in children in Uganda: a case-control study

Version: 3 Date: 11 October 2010

Reviewer: James Berkley

Reviewer's report:

The manuscript deals with an important topic. Whilst there is reasonable understanding of the interactions of HIV and malaria in adults, there are few well conducted studies among children. The manuscript is clear and well written, the hypothesis is clear and the study design is appropriate. Definitions used are sensible and appropriate. Limitations are appropriately discussed.

Essential Minor Revisions:

The children with cerebral malaria were younger than those uncomplicated or no malaria. Since both incidence of cerebral malaria malaria and parasite density has a strong association with age, the odds ratios for these should be adjusted for age as a confounder. I see in the tables that this has been done, but the adjusted odds ratios rather than unadjusted odds ratios should be given in the abstract.

The parasite density results in table 4 should also be adjusted for age, and both the unadjusted and adjusted odds ratios presented in the text. The discussion should focus on the adjusted odds ratios.

Were the actual white blood cell counts available to calculate parasite density? If so, they should be used rather than using 8000 as recommended WHO, since this may be an additional source of bias if counts differ between HIV+ and HIV- children.

In the discussion the statement that ‘... There are no similar studies with which to compare these results....’ is not correct. The finding of an association between HIV infection and severe malaria in Kenyan children against community controls, and an association with the density of parasitaemia was was reported last year (Berkley et al. Clin Infect Dis. 2009 Aug 1;49(3):336-43.). The findings of this study should be discussed in relation to that paper.

I suggest dropping the suggestion under 'limitations' in the discussion for a prospective cohort study becuase cotrimoxazole prophylaxis would be required, reducing subsequent malaria episodes dramatically.

Surely a more important statement in the abstract conclusion is the importance of starting cotrimoxazole prophylaxis, rather than more research on the correlation?
Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests