Reviewer's report

Title: Marked spatio-temporal heterogeneities in human antibody responses to malaria in western Kenyan highlands

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Reviewer: George Ayodo

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With the decreasing transmission of malaria in several parts of Africa and elsewhere, studying malaria exposure at highland areas with a malaria intensity cline is critical for effective malaria control. Thus, this paper attempts to provide some interesting information on micro-geographic risk of malaria.

Major Compulsory Revisions

The study investigates serologic evidence of malaria exposure at highland sites along a malaria transmission intensity cline. However, there are major compulsory revisions on study design and analyses.

1. Other studies have shown that antibody responses to MSP1 lasts for more than a year (Drakeley et al, 2005) and thus using it as a marker to assess variability of malaria exposure between rainy and dry seasons may have several limitations. Furthermore, Figure 2 shows that there is no difference in the prevalence of P. falciparum during rainy and dry seasons, suggesting continued transmission. This complicates assessing exposure using a serologic marker. Indeed Table 1 supports the complication because there is lack of any difference in exposure between rainy and dry seasons. It is therefore important that the authors state the potential limitations of using a serologic marker, in particular MSP1, in this study. Alternatively, the authors can improve the result by including relatively shorter longevity serologic marker.

2. The number of study participants based on locality are clearly noted but it is missing for age categories, e.g for <5, n=?, for 5-14 years, n =? and for # 15 n =?. On Figure 1, the number of study participants in highland uphill, highland valley bottom and lowland during dry season are 178, 136 and 74, respectively. However, on Figure 4, the number of study participants is not indicated. On counting the points on the graph, n ~ 34 for uphill, n ~ 26 for valley and n ~ 65 for lowland for dry season. It is also not clear how the study participants were selected for the analysis e.g how 34 were selected from 178 in uphill cohort etc. Without clear explanation of this, an interpretation of this result may be misleading.

3. Figure 3 shows a difference of IgG titers among different localities stratified by age. The P values show differences across age groups e.g. between 5-14 years and 15+ years. Given that response to serologic markers are age dependent, it would be good to compare responses as per the age categories e.g 1-4 years in
the uphill compared to 1-4 years group in the valley. By doing this, authors can coarsely say that age is matched between the localities. Overall, the best approach would be to control for age during the analyses.

With the above concerns, it is unclear if age-specific MSP1 seroprevalence, seroconversion rates and total IgG titers have demonstrated a highly heterogeneous human exposure in western Kenya. I therefore recommend major compulsory revisions based on the above concerns

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests