

MS title: Malaria pattern observed in the highland fringe of Butajira, Southern Ethiopia: a ten year retrospective analysis from parasitological and metrological data

COMPULSORY

1. **Reviewer comment:** P.2, 2nd para: I do not understand why the unstable nature of highland malaria causes a high prevalence rate. I would think that the prevalence is low in comparison with lower lying areas, but that due to lower immunity; the epidemic potential is high (as mentioned as well). Please clarify and/or adjust.

Response: we accept the comment so we adjust as a reviewer comment (Page 2nd paragraph 2).

2. **Reviewer comment:** last para: here the authors present their hypothesis explicitly and then tell how they aimed to test this hypothesis. The hypothesis states that malaria transmission in the highland areas of Ethiopia is autochthonous because of the repeated nature of the epidemics. For a thorough evaluation of this hypothesis, it would be necessary, in my view, to include malaria vector studies as well. Autochthonous transmission would imply that *local* malaria mosquitoes become infected with malaria parasites and infect people *locally*. Why were these studies not undertaken or incorporated here? This should be explicitly addressed in the Discussion

Response: Page 4 last paragraph we include parasitological and entomological studies done in the study area and in this way we adjust our explanation as reviewer comment.

Reviewer comment: mention under Data analysis that correlation analyses were also done at one month time lag as reported in Table 2. And what screening significance did the authors use for inclusion of factors from the bivariate (Spearman) correlations into the multivariate linear regression.

Response: we include one month lagged effect in data analysis part as a review comment and the inclusion criteria as explain in the manuscript the linear regression was done to know the multiple effect of the independent variables on the outcome variable(we also include this in amended manuscript ,Page 7).

3. **Reviewer comment:** P.8: here it becomes clear that *P. vivax* is a very prominent cause of malaria in the Butajira area. Therefore, some attention to the differences between *P. vivax*

and *P. falciparum* should be paid in the Introduction. The point also comes back in the discussion

Response: thanks for the comment, we accept it. In page 4 of the revised manuscript we add the prevalence of the two *Plasmodium* species and in discussion part we also try to explain the rise of *Plasmodium vivax* in the study area.

4. **Reviewer comment P.11:** the authors concluded that they have provided evidence for the existence of locally contracted malaria. This is really cutting corners here, because the authors have not considered the role of the mosquito vector or the role of people's migration patterns (i.e. do they travel to lower areas and contract malaria elsewhere).

Response: the authors believe that malaria is locally contracted in the highland fringe of Butajira because of the presence of vectors responsible for the transmission of malaria in Ethiopia is collected from this fringe area in our previous entomological study. The presence of malaria in people who had no travel history is also checked by our previous parasitological study (Tesfaye et al. Malaria Journal 2011, 10:153) and other study done in the same site. In the revised manuscript we try to explain this situation by referring the above previous works.

5. **Reviewer comment:** the authors mention that they did not find significant associations between climatic variables and malaria cases in their study and compare this with studies from other parts of the world that are in agreement with their findings or not. However, they do not explain why they think there were no significant associations. Is this a matter of power in the data (should more years be considered?), a matter of statistical tools used or is there really no association (and is climate thus not a driving force)?

Response: we accept the author comment and we add our explanation on page 14 of the revised manuscript.

6. **Reviewer comment Figure 3:** I do not see the added value of this Figure as it plots the same as Figures 1 and 2, but then together in one graph. Moreover, it cannot be used to judge whether there is or there is no correlation between variables as it is simply too crowded

Response: we accept the comment and we drop the figure.

ESSENTIAL

The authors would like to thank the reviewer for the comments and all comments which were given in this part are also incorporated in the revised manuscript.

Optional

1. **Reviewer comment** P.3: 3rd para: the review of Chaves & Koenraadt (Q Rev Biol, 2010) comes to a similar conclusion that there was evidence of a significant warming trend in western Kenya based on several (statistical) models. However, this paper also calls for thorough consideration of other (ecological) factors that contribute to changing trends in malaria transmission.

Response: the author believe that the 10 years malaria and climatic data does not show the effect of climate on the rise of malaria in the study area because malaria was already established in this area but if more than 10 years data were available the effect of climate specially temperature has effect on the emergence or resurgence of malaria in the study area. We included this in our explanation in the revised manuscript.

2. **Reviewer comment** P.4: give a bit more background on what the Pawie settlement scheme and the development activities in the township of Arbaminch entailed in order for the reader to know how these activities could affect malaria.

Response: thanks for the comment, the authors drop the whole statement about Pawie settlement and the development activities in the township of Arbaminch because the area are malarious lowland area.

3. **Reviewer comment** P.7: the authors mention to have collected data on Coartem implementation and other malaria control activities. However, in the Results they do not report when and where these activities have taken place and how they could have affected the malaria transmission pattern. Were they included as variables in the regression analyses? For example, I could imagine that the 10-year data set could be divided into a *before* and *after* Coartem implementation and analyzed as a factor as such. In that regard,

the data analyses were limited to the possible effects of only four variables: monthly rainfall, maximum temperature, minimum temperature and average temperature.

Response: we include the time of implementation of Coartem in the result section on page 8.

4. **Reviewer comment:** what do the authors mean by saying that ‘Annual variation of total rainfall, was not statistically significant ... unlike inter annual malaria magnitude’? Here, the manuscript could benefit from some more interpretation of the results already rather than just listing the statistical results. For example, “Over the 10 years of study, annual rainfall was relatively constant, as demonstrated by the lack of significant interannual variability in total rainfall ($P = \dots$ etc.). As a result of seasonal effects, monthly rainfall did vary considerably over the year. This can be seen from the significant inter monthly variation ($P = \dots$ etc.)”

Response: for the comment we try to adjust the section to biological sound instead of listing statistical analysis.

5. P.13: 2nd para: this is a repeat of (or at least very similar to) what was already said on page 12. Please integrate these paragraphs.

Response: in our view the explanation on page 12 is about the impact of rainfall on distribution of malaria whereas Para 2 of page 13 is about the impact temperature on transmission of malaria. If necessary we would combine the two paragraphs.

New addition

1. We changed the R squared into Adj R squared in the linear regression analysis in the cumulative effect of rainfall, minimum and maximum temperature. In the same way instead of reporting R squared our biostatistician recommended reporting regression coefficient (Beta) Page 10 and abstract section.