Reviewer's report

Title: In vitro antimalarial susceptibility and molecular markers of drug resistance in Franceville, Gabon

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Reviewer: Christian CH Happi

Reviewer's report:

General Comments.

This is manuscript that is describing in vitro susceptibility of Plasmodium falciparum to antimalarial drugs and the association between parasite genes polymorphisms in vitro drug response in a malaria endemic area of Gabon.

The manuscript is well written and is addressing an important aspect of malaria control. The methods and data analysis are well described and appropriate. However, the sample size of the study is small and the discussion seems not to be well balanced and supported by the data.

Overall, manuscript has both minor essential and major compulsory revisions that the authors must address before acceptance to publication.

Minor Essential

Results:


-Line 2 of this paragraph refers to figure 1. This figure does not exist, and therefore this statement should be removed.

-The number of samples is not indicated for all proportions reported in the text. N=11 is reported only for DHA and this should have been the case for all antimalarial drugs being reported in this section of the manuscript.

2. Drug sensitivity and Plasmodium falciparum gene polymorphisms

-The title of Table 4 should change as it gives the impression that all isolates are in the drug sensitive groups.

- Lines 3-6 in this paragraph has to be recasted, it is quite difficult to comprehend the message being conveyed by these statements.

Major Compulsory:

1. Because of the small sample size of the study presented in this manuscript, I will recommend that the manuscript be rewritten and presented as a short report for further review.
Discussion:

2. The authors have reported cross-resistance between several antimalarial drugs in vitro. However, at no point during the discussion this very important aspect of the result is thoroughly discussed. Especially in the context of polymorphisms of genes that have been found to be involved in the mechanisms of resistance to various antimalarial drugs. In addition, the history of antimalarial drugs used has been demonstrated to be very important in cross-resistance to antimalarial drugs. These are important issues that are missing in the discussion of this manuscript.

3. The authors found that mutant pfmdr1 Y1246 allele are higher in CQ sensitive that CQ resistant isolates, and yet in the discussion they say that they found an association between CQ resistance and pfmdr1 Y1246 allele. This discrepancy between the result and the discussion should be addressed.

4. The authors did not analyze the pfmdr1 F184 allele in the context of this manuscript. However, in the discussion of the manuscript they recommend surveillance of resistance to artemether-lumefrantrine, based on the assumption that the pfmdr1 F184 allele is important to parasite reduced susceptibility to this ACTs. The recommendation of the authors is not based on scientific evidence and should therefore be removed from the discussion of the manuscript.

5. A large proportion of P. falciparum from Franceville in this study was shown to harbour the pfcr7 CVIET haplotype. However, at no point in the discussion of the manuscript the high prevalence of this haplotype was discussed with susceptibility to MDAQ or the use of AQ as a partner drug in ACTs in Gabon.

6. The authors suggest the need for molecular surveillance with respect to in vitro sensitivity. However, an association between gene polymorphisms and in vitro susceptibility has been demonstrated only pfmdr1 Y1246 and MDAQ. I will suggest caution based on the data from this study.

Discretionary Revision:

It would have been great to investigate the impact of genetic background of pfmdr1 and pfcr7 polymorphisms on in vitro response of P. falciparum as well as the interaction between these genes and susceptibility of parasites to various antimalarial drugs.

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

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

I declare that I have no competing interests.