Reviewer’s report

**Title:** Diagnostic utility of zinc protoporphyrin to detect iron deficiency in Kenyan preschool children: a community-based survey

**Version:** 0  **Date:** 27 Feb 2017

**Reviewer:** Crystal Karakochuk

**Reviewer's report:**

This is a well-written manuscript describing a study in Kisumu-West district of Kenya. Authors aimed to identify factors associated with ZPP concentrations in young children (1-3 years) and to assess the diagnostic ability of ZPP (alone or with Hb) to identify iron deficiency.

I have few comments and suggestions for the authors.

1. The proportion of children with whole blood ZPP >70 umol/mol haem was very high (98%) similarly, erythrocyte ZPP >40 (97%). The authors describe in lines 349-356 how plasmodium infection causes elevated ZPP and further in lines 357-360 the suspected mechanism of a haemolysis-induced increase in erythropoietin activity in the presence of malaria that drives the demand for iron. Given these mechanisms, I'm curious to ask about the known prevalence of sickle cell, thalassemia, or glucose-6-phosphate dehydrogenase deficiency in this study population - could these factors be contributing to the surprisingly high levels of ZPP observed in your study?

2. How did you assess/approach QC in the ZZP method? Has your method for ZPP been previously validated? (if so, can you provide details or reference).

3. The authors clearly state why children with inflammation were excluded from some analyses (lines 366-70) and why other methods of correction were not applied (lines 372-386). Inflammation was assessed based on AGP and CRP biomarkers (which is pretty standard) - how accurate do you think these biomarkers capture inflammation (especially among populations where infection is persistent and recurrent). Although I realize this is global standard practice to use these two biomarkers, I wonder, could this be a limitation in your conclusions?

4. The exclusion criteria in lines 111-4 is not completely clear. 'Not at risk of malaria (e.g. children who received chemoprophylaxis against malaria because of HIV infection or sickle cell disease) - previously it was mentioned in inclusion criteria: absence of reported or suspected major systemic disorder. So perhaps the latter statement is not necessary. And
second, "did not complete the second and third doses of dihydroartemisinin-piperaquine'. Please clarify.

Minor points:
Line 95: , should be .
Line 94: Is this region at sea level (<1000m)?
Line 103: Suggest to use 1-3 y for consistency (rather than 12-36 mo)
Line 116: Was blood fasting?
Line 119: Was Hemocue also done in triplicate (or just ZPP). Or was Hemocue Hb measured just once.
Line 124: What type of rapid kit was used.
Line 126: 'Further details are reported elsewhere.' - Please can you include a citation here.
Line 151: CRP and AGP are acronyms here but spelled out throughout the most of the manuscript.
Lines 469-70. Suggest to remove 'If asked, we can elaborate on our reasons with Editor'
Line 465: Period needed at end of sentence.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.
I am able to assess the statistics

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Please indicate the quality of language in the manuscript:

Acceptable

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