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LETTER TO THE EDITOR

Response to "Lactation Status and Studies of Pyrimethamine Pharmacokinetics in Pregnancy"

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To the Editor:

We thank Dr Salman and Professor Davis[1] for their comments on our publication on the pharmacokinetics of sulfadoxine-pyrimethamine in African women during pregnancy and postpartum.[2] We reported that, compared to during pregnancy, pyrimethamine clearance was 18% higher postpartum, with large variability in the data across the four study sites, which sampled the patients at different times postpartum. In the Letter to the Editor by Salman & Davis,[1] they suggest that lactation status could explain the increased clearance postpartum and our result would, therefore, not contradict findings in other studies using nonpregnant women as a control group.

We agree that lactation status could be a possible contributing factor for the increased clearance postpartum. Lactation was considered as a possible reason for the faster clearance after delivery and for the differences between sites, but no information on the lactation status of women during the postpartum period was available, so we were not able to test this hypothesis. The effect of lactation is expected to gradually dissipate as more women stop breastfeeding, but lower clearance was not observed in sites with later postpartum sampling (up to 63 weeks). Further, there is large variability in the amount and frequency of breastfeeding, which would affect the prolactin levels that could alter drug metabolism.[3] In Africa, the highest rates of exclusive breastfeeding are currently found in Eastern/Southern Africa (47%) and the lowest in West/Central Africa (28%).[4] Additionally, as we reported in ref. 2, hematocrit data were only available at dosing, but longitudinal changes are possible and could not be accounted for in the model. The prevalence of postpartum anemia in developing countries is in the range of 50–80% due to prepartum iron deficiency, acute bleeding at delivery, folate and vitamin B12 deficiency, and inflammatory, infectious disorders.[5] These factors could all be confounders contributing to the between-site differences, which would need to be considered in quantifying the effects of lactation on clearance.

In conclusion, we agree with Salman & Davis[1] that careful considerations should be taken in selecting an appropriate control group for pharmacokinetic studies in pregnancy and we suggest collecting information about breastfeeding and the other confounders identified above and extending the follow-up period until after weaning. As the postpartum pharmacokinetics may not be equivalent to that in nonpregnant women, and World Health Organization guidelines recommend breastfeeding up to 2 years of age, postpartum women are an important subpopulation and should not be neglected in the evaluation of antimalarials.

Conflict of Interest. K.I.B. is a member of the World Health Organization (WHO) Technical Expert Group (TEG) on Malaria Chemotherapy and of the WHO TEG on Drug Resistance and Containment. The remaining authors declare that no competing interests exist.

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