Review of: "Misdiagnosis of Dengue Fever as Malaria and Typhoid Fever and Their Co-infection in Rural Areas of Southwest Nigeria"

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Potential competing interests: No potential competing interests to declare.

The manuscript submitted by Dr. Okoror et al. is entitled: Misdiagnosis of Dengue Fever as Malaria and Typhoid Fever and Their Co-infection in Rural Areas of Southwest Nigeria.

The authors aimed to assess the misdiagnosis of Dengue as malaria or typhoid fever in a rural cohort of patients from Southwest Nigeria. This study holds significant importance as there is limited understanding of Dengue prevalence in Nigeria, and misdiagnoses of Dengue and malaria pose substantial challenges in Africa and Asia. Additionally, the southwest region of Nigeria appears to be conducive to the co-circulation of Dengue, malaria, and typhoid fever. While the authors effectively address key points, further clarifications are needed to underscore the significance of the results obtained in this study.

<u>Methods</u>: Overall, the method section of the manuscript requires substantial clarification. It is challenging to discern the specific procedures for each assay, and there is a need for clear referencing of all tests and reagents, including catalogue numbers or references for identification (e.g., RDT tests, ELISA kits). Additionally, it is unclear how concentrations were calculated and their relevance to the study objectives. For instance, the significance of the concentration of NS1 antigen and anti-DENV IgM (Figures 1 and 2) is not well-explained.

Several points require more details from the authors. For example, the inclusion criteria lack specificity, particularly regarding febrile illness or other symptoms. The term "people seeking malaria/typhoid diagnosis" is vague and cannot serve as an inclusion criterion. The study design is also ambiguous, particularly concerning whether RT-PCR was conducted on all patients or only those with positive malaria/typhoid diagnoses.

The paragraph added regarding NS1 in the study design requires accuracy or further clarification. NS1 is not included solely to support IgG or IgM; instead, a combination of NS1, IgM, and IgG is used for dengue diagnosis. It is known that both antibody and antigen levels vary with the timing of infection and sample collection. Additionally, anti-DENV IgG can result from either past or current infections.

Figures & Tables: The absence of figure legends for Figures I-VI impedes the interpretation of the figures. Including figure legends would greatly improve the clarity and understanding of the data. Additionally, none of the graphs include a limit of detection, making it unclear what values are considered high and why. Providing this information would enhance the interpretation of the results.

It would be beneficial to include the distribution of all three diseases in terms of season (rainy, dry, etc.) throughout the year, rather than just a monthly distribution. This additional information would provide a more comprehensive understanding of the seasonal patterns of disease incidence. Furthermore, a table summarizing the demographic distribution of all participants is missing, which would provide important context for interpreting the results.

Regarding the literature cited for malaria-dengue co-infection, the chosen articles may not be the most relevant or informative. It would be beneficial to consider including more recent and pertinent literature on this topic to develop the discussion of malaria-dengue co-infection.

Overall, I believe addressing these points would enhance the clarity and completeness of the manuscript.