**Author’s response to reviews**

**Title:** Nasopharyngeal carriage, spa types and antibiotic susceptibility profiles of Staphylococcus aureus from healthy children less than 5 years in Eastern Uganda

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**Version:** 1  **Date:** 02 Aug 2019

**Author’s response to reviews:**

29th July, 2019

To the Associate Editor,
BMC Infectious Diseases

Dear Professor Adebayo Osagie Shittu PhD,

RE: Resubmission of INFD-D-19-01209: Nasopharyngeal carriage, spa types and drug susceptibility profiles of Staphylococcus aureus from healthy children under 5 years in Eastern Uganda

We thank you for your comments prior to sending our manuscript for peer-review. We found the comments to be useful and we have fully addressed all of them and made the necessary corrections to manuscript. We confirm that our revised manuscript conforms to the journal style, and we hope that you will find it suitable for publication in your esteemed journal.

We look forward to hearing from you soon concerning this.

Regards,
David P Kateete, Ph.D., Makerere University

POINT-BY-POINT RESPONSE TO THE COMMENTS
General comments

The manuscript is well-written, however, a number of adjustments are suggested.

COMMENT:

1. Table 1 is a large table – it should be presented as supplementary data.

RESPONSE:

As advised, the large Table 1 is now presented as a supplementary file (Table S1).

COMMENT:

2. It would be nice if the authors could show the various antibiotypes of the MSSA and MRSA, and the relationship (if any) between the antibiotypes, PFGE groups and spa types.

RESPONSE:

As advised, antibiotypes of the MSSA and MRSA isolates and their relationship with Spa and SCCmec types are now shown in the resubmitted version (see Table 1). There was no meaningful relationship between the antibiotypes and PFGE groups hence these associations are not shown/discussed.

COMMENT:

3. Information on the PFGE profile of the strains are not included in the result section. Is Figure S1-1 the PFGE profile for select strains? Lines 132-139 suggest that PFGE analysis was performed on all the strains.

RESPONSE:

Yes. Figure S1-1 depicts the PFGE profile for select strains as we could not perform this procedure for all the isolates. We have revisited Lines 132-139 to clarify this and we have also discussed it among the limitations.

COMMENT:

4. A number of atypical S. aureus strains (e.g. nuc negative) were observed in this study, possible these could be S. argenteus?

RESPONSE:

We thank you for bringing this to our attention. We regarded the nuc negative isolates to be S. aureus as the Phoenix ID that we used as a tie-breaker confirmed them as so however, literature indicates that the Expert Identification systems such as the Phoenix ID can also fail to distinguish the two species, see https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4298100/ So, it is possible that these isolates could be S. argenteus but as we did not confirm them to species level, we have retained their identity as S. aureus but discussed the possibility that they could have been S. argenteus species misidentified as S. aureus and in future investigations in this setting should consider this possibility.
COMMENT:

5. A limitation of the study was the use of http://spatyper.fortinbras.us/ for the identification of the spa types (a number of unidentified spa types) and lack of information on the clonal complexes based on MLST. These limitations were not mentioned in the manuscript.

RESPONSE:

The official Spa type server (Ridom) requires subscription (fee for service) hence we could not use it as we lacked funds to pay for access. Therefore, we used the http://spatyper.fortinbras.us/ server as it is freely accessible and other investigators have used it to accurately determine spa types. However, we verified all the repeats and genotypes with the Ridom database for conformity. We also pointed out in the manuscript that the http://spatyper.fortinbras.us/ is not the official server for determining spa types, and discussed it and the lack of information on the clonal complexes based on MLST as limitations.

Specific comments

COMMENT:

a. Line 30: etc.?

RESPONSE:

Here we intended to say that there are several factors (e.g. country, demographic group, sex, profession, etc.) that can influence the S. aureus carriage rates and we mentioned only a few for space reasons. The sentence has been revisited for clarity.

COMMENT:

b. Line 124-125: These cefoxitin-susceptible but mecA positive strains were not indicated in Table S1.

RESPONSE:

Initially, the 12 mecA-positive S. aureus isolates were considered to be cefoxitin susceptible based on the disc diffusion method. However, further investigation based on MICs revealed that MICs for these isolates fell within cefoxitin resistance according to CLSI, and they were regarded cefoxitin resistant henceforth. These isolates were also confirmed to be MRSA by the automated BD Phoenix 100 ID/AST expert system.

COMMENT:

c. Lines 163, 168, 174, 179, 180, 181, 182, 186, 191, 192, 194, 197, 202, 206, 208, 211, 214: I am not clear with the style of the authors in the manuscript with a statement like ‘Figure 1 & Additional file 1: Table S1’.

RESPONSE:

We have revisited the figure/table citations for clarity.
The sentences beginning with the “Note” have been rewritten for clarity.

The sentence has been rewritten as advised.

As advised, the sentence has been rewritten for clarity.

The sentence has been rewritten to indicate that mupirocin is also used for nasal MRSA decolonization of patients.

The first published report on S. aureus infections in Uganda was in 1958. Please see https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2026807/

All isolates that were successfully sequenced have spa repeats indicated in Table S1. However some
isolates, although previously characterized, were found to be missing while others did not grow on sub-culturing.

COMMENT:

j. t3092 is not among the spa types for MRSA in Table S1.

RESPONSE:

Spa type t3092 is among the spa types for MRSA in Table S1, see column AE / line 130, isolate # 128 / isolate ID R-28. We thank you.