Reviewer's report

Title: The influence of Streptococcus pneumoniae nasopharyngeal colonization on the clinical outcome of the respiratory tract infections in preschool children

Version: 2 Date: 18 February 2015

Reviewer: Nicole Wolter

Reviewer's report:

Major Compulsory Revisions

1. The biological hypothesis of this study is not clear. As stated by the authors, the pneumococcus commonly colonizes the nasopharynx of young children without causing disease. Therefore detection of the pneumococcus from a NP swab may be an indication of the pneumococcus being the cause of the RTI, or may not, and may be that the organism is just being carried. The authors did not test for any other common respiratory pathogens, and therefore cannot assume that the detection of pneumococcus in the nasopharynx is indicative of pneumococcal disease. Please can the authors clarify their biological reasoning behind how pneumococcal colonization is associated with recovery time, clinical symptoms, use of antimicrobials etc. It is hinted at in the discussion that the authors hypothesize that colonization with the pneumococcus increases ones risk of pneumococcal disease, and it is therefore assumed that the authors used pneumococcal colonization as a proxy for pneumococcal disease? Please clarify this in the manuscript, preferably in the earlier parts such as the introduction and methods. The limitations associated with this inference, need to be stated in the discussion.

2. Background, third paragraph: Day-care centre attendance and young siblings are known to be risk factors for pneumococcal colonization, and these studies should be referenced in the background section. However, as the pneumococcus is commonly asymptomatically carried, it is not clear how the authors propose that it may be associated with recovery time, symptoms etc. Please could the authors clarify their hypothesis.

3. Results, Figure 1: Please can the authors explain their reasoning in this analysis – is it the assumption that if the pneumococcus is detected in the nasopharynx that it is the cause of the RTI? If so, this is not plausible as pneumococcus is known to be carried, specifically amongst the age group studied. If not, then please can the authors explain the relevance of figure 1.

4. Results: throughout results, data in the form of numbers (n/N) should be provided and not only the percentage results.

5. Discussion, first paragraph, third sentence: please can the authors explain this sentence as the pneumococcus is commonly carried amongst healthy individuals. It is not colonization, but rather pneumococcal disease that affects health.
6. Discussion, first paragraph, fourth sentence: it is my understanding that colonization does not affect the course of a disease in the carriage state and that it will only affect the outcome if it develops into disease either as the primary or secondary infection. The authors did not identify the prevalence of other common respiratory infections in this study, and did not examine the difference in the course of the RTI in patients with and without pneumococcal colonization.

7. Discussion and abstract conclusion, first sentence: the statement that Spn nasopharyngeal colonization has a negative impact on the course of RTI need to be more clearly explained as it is not the colonization itself that causes the negative impact but rather that Spn colonization increases ones risk of pneumococcal disease, and this in turn, has a negative effect on the course of RTI.

8. Abstract, results: Data in the forms of numbers (n/N) need to be provided to justify the statements made. Include only the most important results of the study in the abstract and provide all the data to support the results.

9. The manuscript would benefit from general language and grammar editing.

Minor Essential Revisions

1. Background, second paragraph, first sentence: It is not clear what is meant by this sentence as the role of pneumococcus as a cause of severe disease is well understood and proven. Recent studies have been focused on the ability of the pneumococcal conjugate vaccine to prevent pneumococcal disease.

2. Methods, first paragraph: Did the enrolment criteria include upper- and lower-respiratory tract infections?

3. Methods, second paragraph: What duration of symptoms was used as a cut-off to meet the criteria of acute infection?

4. Can the authors clarify the use of the pneumococcal conjugate vaccine in their country – is it used as part of routine infant immunization program, what is the vaccine coverage in the country?

5. Italicise names of bacterial organisms in the references

6. Table 1: This table should be renamed as it does not give the demographic data of enrolled patients but rather number of patients and the prevalence of pneumococcal colonization by site. Alternatively, additional demographic data should be added to this table such as mean age of children by site etc.

7. Results, second paragraph: The details of the results of the Poisson regression analysis need to be shown to qualify the last sentence in this paragraph.

8. Table 2: the actual result numbers (n/N) need to be added to this table to support the results obtained.

9. Figure 1 and Figure 2: Please clarify the y-axis on this figure as the title is Cases per serotype, and yet the axis is measured in percentages?

10. Results: Please clarify what “G+” as a serotype is?
11. Figure 1 and 2 and corresponding legend: the asterisk denotes significant
difference in what between the serotypes indicated and the spn-negative cases?
This should be clarified in the figure legend.

12. Results, recovery paragraph, last sentence and Figure 1: It is not clear how
serotypes 15, 23 and 6A were significantly associated with longer disease
duration compared to spn-negative cases when all of the patients infected with
these serotypes recovered within 4 weeks.

13. Figure 1, Figure 2 and Table 3: please clarify the difference between
serotypes 23F and 23.

14. Table3 and results, serotypes paragraph, first sentence: Please check this
sentence as there were more 6B cases than 3 and 18C, and yet these have not
been mentioned in the text.

15. Table 3 and results, serotypes paragraph, fourth sentence: This is because
URTI was the most common diagnosis (n=592). The prevalence of serotype G
was actually only 2% (13/592) amongst URTI cases.

16. Results, antimicrobial use paragraph, first two sentences: The relevance of
the use of antimicrobials 1-6 months prior to sampling is not clear. This did not
appear to be an objective of this study as all patients that had received prior
antibiotics in the 1 month period prior to sampling were excluded from enrolment.

Discretionary Revisions
1. Methods, fifth paragraph: a reference should be provided for the standard
culture methods used.

2. Table 1: a chi-squared test of the prevalence of pneumococcal colonization by
site would be useful to identify whether there were significant differences by site.

3. Results, DCC attendance paragraph: a more accurate term for “rate of spn
colonization” is “prevalence of spn colonization”, as the term rate implies the
speed at which it happens.

4. A useful analysis would be to determine the predicted coverage of the
pneumococcal conjugate vaccine against colonization, based on the serotypes
detected.

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being
published

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