Reviewer's report

Title: Invasive bacterial infection complicating malaria in African children: a systematic review

Version: 1 Date: 1 March 2013

Reviewer: Malcolm Edward Molyneux

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MAJOR COMPULSORY REVISIONS

1. Methods #1 comes closest to a definition of the study, indicating a systematic search for ‘articles describing bacterial infection among children with P falciparum malaria.’ The title of the paper suggests a slightly different review topic, namely ‘invasive bacterial infection (IBI) complicating malaria...’ This wording implies a conclusion about the nature of the relationship between malaria and IBI (ie that the malaria came first and paved the way for the IBI), which seems premature in a title. It would be helpful if the review could have an early paragraph clearly defining the subject-matter of the review, and the title could then be adjusted accordingly (if it still seems necessary).

2. In the Abstract (and frequently elsewhere in the paper), causality is assumed or implied, when this is not justified. ‘Bacterial co-infection resulted in 3-fold higher case fatalities’ (Abstract) and ‘62% of bacteraemic paediatric admissions were attributable to malaria’ may be true in statistical language, but not necessarily in terms of biology or pathogenesis. Similarly in the section headed ‘Mortality in malaria and IBI co-infection’ there is the statement: ‘In Mozambique, an even more substantial effect of IBI co-infection on malaria mortality increasing from 4% to 22% (P < 0.0001)’, the same distinction between statistical and biological terminology should be borne in mind. Please avoid use of statistical terms that might prompt the reader to think that biological causality is established.

3. Table 1 does not include a column for prevalences of IBI in non-malarial control or comparator groups in populations or among patients. It would be helpful to have such a column, and to have this aspect discussed more in the text. In 4 studies in Table 1, a prevalence of IBI in ‘non-malaria’ is given, seeming to imply that the other studies in Table 1 did not have a non-malaria comparator group. [In those with a non-malaria group for comparison: in 2 studies, prevalences of IBI in malaria and non-malaria are similar; in one study the prevalence of IBI is much higher, and in the other study it is much lower, in the non-malaria group than in the group with malaria].

4. #s 3, 4 and 5 of Discussion state thoroughly the problems involved in attempting to understand (a) whether there is a relationship between parasitaemia and bacteraemia and (b) what, if there is one, it means for policies and treatment guidelines. The transition from these guarded and cautious arguments to the seemingly confident ‘Conclusion’ paragraph is less convincing.
In my view, in the first sentence under ‘Conclusion’, ‘...results in’ could be changed to ‘...in turn is linked with’, without damage to the argument, and without altering the recommendations made in the remainder of the final paragraph. [My wording is only a suggestion - something else along the same lines would be acceptable]

MINOR ESSENTIAL REVISIONS

5. Occasionally the word ‘incidence’ is used where ‘prevalence’ is meant – eg ‘Evidence from Clinical Studies’ # 3 ‘the incidence of malaria parasitemia in children with bacteremia’ and Discussion # 3: ‘those studies reporting high incidences of staphylococcal organisms.’

6. It would be helpful to have a clearer distinction made between P falciparum parasitaemia and ‘malaria’ (as an illness, mild or severe). There is not enough discussion of the phenomenon of asymptomatic parasitaemia [briefly mentioned in Discussion], which may have been prevalent in up to half the population of children in some areas where studies of IBI have been done.

7. Some references are repeated (eg 16=41, 19=34)

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests