Reviewer’s report

Title: Severe imported falciparum malaria among adults requiring Intensive Care: a cohort study.

Version: 3 Date: 2 December 2012

Reviewer: Thomas Zoller

Reviewer’s report:

General: this is a good retrospective review of a single-center cohort of patients with imported severe malaria. The manuscript adds relevant information to understanding the clinical presentation of this disease in a non-endemic setting, but my overall impression is that the information could be presented in a better and more systematic way, giving more valuable information to the clinician as well as making better use of the data collected.

- Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)

- p1 title: ….: a cohort study. A cohort study in most cases refers to prospectively defined cohorts. In order to make clear that inclusion criteria have been defined retrospectively, I suggest to classify the study as a retrospective cohort study and to amend the title accordingly.

- Abstract line 1: …AKI occurred…The abbreviation AKI is not as common as e.g. ARDS in medical literature. I suggest to spell out AKI here.

- Abstract: to me, one of the key messages of the manuscript (identical with personal experience) is that patients with imported severe malaria rather die from secondary intensive care and/or infectious complications than from malaria itself. This central finding mentioned in the outcome should be included in the the abstract, and maybe also discussed in the conclusions section. This may lead to physicians having a low threshold for early antibacterial treatment where secondary infection cannot be ruled out clinically.

- Complications of malaria: it would be very interesting to know if those patients developing ARDS had concurrent evidence of bacterial infection. Since ARDS due to malaria is rare and ARDS secondary to bacterial infection, sepsis or pneumonia is common in these patients, the authors may want to explore the dataset for factors discriminating between these causes of ARDS or give a clinical estimate of the likely source of ARDS, improving the clinical value of the manuscript.

- Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

- Outcomes line 5: “All” – please make clear that the following sentence refers to
those who died.

- Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)

- Management: there is only very little information on antimalarial treatment used. Of interest would be information on treatment duration, policy of changing to oral therapy, source of i.v.-quinine and artesunate (since these drugs are difficult to obtain), partner antimalarial drugs used. I consider this information as essential for the manuscript, as it would enhance its value for doctors with less experience in malaria treatment. Which local criteria were applied for initiating exchange transfusion? (given in the discussion, but should be mentioned earlier).

- Complications of malaria, last sentence: I do not understand what “in parallel” refers to; it reads better if it is omitted. I am not sure about the value of the statement made in this last sentence in this paragraph; in any way one would expect to give at least a numerical / statistical information illustrating the differences in parasitaemia at the time of occurrence of the respective complications, if this difference is considered relevant by the authors.

- Complications of malaria, second paragraph: in order to make it more illustrative for non-malaria experts the typical and important complication of hypoglycaemia could be better described by giving an example value or average value of glucose of patients diagnosed with hypoglycaemia.

The same applies to “coagulopathy” and “bleeding”. Although this is a defined WHO-criterion by its own, this clinical paper should give more information on what was seen in clinical practice, e.g. DIC or bleeding due to thrombocytopenia? In addition, other than citing the WHO criterion, there is no definition of coagulopathy or bleeding given in the methods section.

- Co-infections, second paragraph and table 3. I am not sure if table 3 is needed. The first part is entirely mentioned in the text, the second part is of limited value. I suggest to name the top three pathogens in the text and omit table 3.

- Outcomes, line 10: has the possibility of quinine inducing cardiac arrhythmias been considered here?

- Outcomes: I miss a table detailing the outcomes of the cohort, making the presentation of this information more systematic. Since this is the core information of the manuscript, and all numbers are written in the text, it is difficult to get an overview of the outcomes, possible underlying reasons and potential risk factors. Of particular interest are those who died; I suggest to make a separate table or section of a table detailing the complications, clinical characteristics (e.g. parasitaemia) and cause of death for this group of patients and give only summarizing descriptions in the text. A negative risk factor analysis in univariate or multivariate analysis does not argue against this.

- Outcomes: to improve the clinical value of the manuscript and since this is only one patient, please indicate here what the clinical presentation of the “post
malaria neurological syndrome” and its outcome was.

- Outcomes: “In logistic regression…”: this output description is very short. Even if the analysis was negative, I suggest to state first that (probably) an univariate analysis was carried out, which variables were included in the logistic regression model (even if it was age and sex only) and then the final result in order to allow the reader to better understand the analysis which was carried out. Given the high number of patients in the analysis, was there any variable of borderline significance? Could you briefly mention in the discussion why probably no factor was found to be significant?

- Conclusions, line 11: “…this report is the first to include patients treated with parenteral artemisinins…”. This assertion is false. There are at least three publications known to me describing cohorts of patients where patients with imported severe malaria are treated with i.v.-artemisinins. I suggest to conduct a new literature search here.

- Conclusions, next page top: “It is possible that the lower mortality at this hospital…. ” I personally do not support such a conclusion statement without carrying out a thorough comparison of underlying populations in French or other studies published, local treatment plans, local healthcare circumstances and any other factor possibly influencing survival. The authors may reconsider this assertion carefully.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I do not have a conflict of interest.