Reviewer’s report

Title: The association between interleukin-6 gene -174G/C single nucleotide polymorphism and sepsis: An updated meta-analysis and trial sequential analysis

Version: 0 Date: 17 Dec 2018

Reviewer: Zorana Dobrijevic

Reviewer's report:

The study used appropriate methodology and the results were consistent with the objectives of the study. Since this meta-analysis is relatively well performed, it only requires minor corrections, together with English editing.

Comments and the suggestions for authors are the following:

- The HWE deviations were assessed, but it should be clarified if studies with significant deviations in controls were considered inadequate for the data synthesis (mainly because of possible genotyping errors), or why was this test conducted if they were still included in the meta-analysis. This issue was discussed in the Discussion section, but should be mentioned also in Results, even though the results of omitting studies with HWE deviations were not shown.

- In the Results section, the search results should be more extensively described with the reference to the flow chart. Also, authors could name the studies excluded after the full-text review in order to allow readers to check the reasons for exclusion.

- The authors should consider changing the term "race" with a more suitable one.

- The terminology in interpreting association the results of association tests should be matched with other case-control studies and meta-analyses (i.e., using "to be associated with", or "to be correlated with", "to increase the risk" instead of "to have a link with…". The same goes for "allele contrast", which could be replaced with "allelic model", or "comparison of allele frequencies", etc).

- It would be more appropriate to present the numerical results of Egger's test instead of graphical representations, since only two plots were shown.

- Some results from supplementary data were introduced in the Discussion section, which is inappropriate. These results are not necessary for discussion, provided that the exclusion of two studies included in the previous meta-analysis is properly discussed and well-argued.

- Information about study design in terms of recruitment of controls could be useful (HB vs PB design, if any with PB) and adequate for subgroup meta-analysis.
Differences between biological aspects of sepsis in neonates, infants and adults could be more widely explained and useful in interpreting the obtained data.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published
Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal