Reviewer's report

Title: Cryptococcal antigenemia is associated with meningitis or death in HIV-infected adults with CD4 100-200 cells/mm3

Version: 0 Date: 19 Nov 2019

Reviewer: Sunil Kannanganat Sidharthan

Reviewer's report:

Authors discuss the results from a prospective study that was conducted in South Africa assessing the increased likelihood of an adverse event (all-cause mortality or cryptococcal meningitis) among people living with HIV (PLHIV) with a CD4 count at baseline between 100-200 cells/mm^3 following a positive screening for cryptococcal antigen. Based on the current guidelines, CrAg screening is reserved for only those with CD4 count <100 cells/mm^3. Authors argue that raising the threshold for CrAg screening to include also cases with CD4 count 100-200 cells/mm^3 likely help reduce the morbidity and mortality in this group of PLHIV especially those living in the cryptococcus-endemic areas.

I have one fundamental issue with the authors conclusions,

Among the 209 participants included in the group with CD4 count 100-200 cells/mm^3, none of the CrAg positive (n=4) and CrAg negative participants (n=205) developed cryptococcal meningitis during the period of follow-up. However, mortality was reported in 2/4 CrAg positive and 11/205 CrAg negative participants. This data was obtained from the South African death registry. Based on the information provided it is unclear that the increased mortality observed in this group is related to cryptococcal meningitis. Given the absence of such an association it is unclear that even if CrAg screening is implemented in this group of people, it would have any benefit to reduce morbidity and mortality.

Minor points:

The acronym used for "people living with HIV" should be uniform across the manuscript. For example, PLHIV is used in abstract, while PLWH is used in the remainder of the manuscript.

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.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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I am able to assess the statistics

Quality of written English
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