OPEN PEER REVIEW

Open Peer Review (OPR)

As a new feature for progressing towards transparency, we decided to open a new window for all of our editors as well as authors titled "**Open Peer Review**". We hope by this new facility, our reviewers will be more motivated and authors will be more satisfied with the review process. We believe that publishing our peer review reports could make a transparent and clear environment for all our efforts within a journal, but not all reviewers tend to publish their comments.

What is "Open Peer Review" process?

An "Open Peer Review" process is making the details of all review process (including reviewers, associate editors, and EICs comments) as "Public" as it is agreed by EIC, Authors, and reviewers.

Advantages of "Open Peer Review" process

- More transparency, constructiveness and tactful comments of the peer review process: leads to an increase in the quality of reviews
- More motivations for all involved roles in the review process
- Authors' satisfactions from the review process: Increases honesty between authors and reviewers
- Education of both authors and new students
- Prevents reviewers from following their individual agendas and leading to the detection of reviewers' conflicts of interests

You can find out more at:
https://sites.kowsarpub.com/kowsar/knowledgebase/category/tree.html#opr.html

Archives of Pediatric Infectious Diseases
Article DOI: 10.5812/pedinfect.101087
Published in: Archives of Pediatric Infectious Diseases: 8(4); e101087

Peer Review Report for "Congenital Infection and Congenital Cataract in Tanzania: A Case Control Study"

Author(s): Furahini Godfrey Mndeme, Tamsyn Derrick, Blandina Theophil Mmbaga, Mchikirwa Msina, Min Kim, David MacLeod, Judith Mwende, Paul Nyaluke, Sonia Vaitha, Matthew Burton, Ursula Gompels, Clare Gilbert, Richard Bowman

Review Timeline:

Submit Date: 25 Jan 2020
Revised Date: 10 May 2020
Accepted Date: 18 May 2020

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (0) 3 Feb 2020

Dear AE,
Thanks for the submission of the “Congenital infection and Congenital Cataract in Tanzania: a case-control study” article.
- Totally this study tries to show the congenital infection in children under 1 year for congenital rubella and CMV infection, but case selection for congenital infection may not be correct and we can not confirm the congenital nature of infection in under one-year-old children.
- Abstract: What HCMV and qPCR and SSA stand for? Please give the full words for abbreviations.
- Material and Methods: Please omit the subheadings in this part. It was better to match the control group by age and weight, because the lower weight in children may accompany congenital disorders so age and weight distribution should be the same in the case and control group.
- Results: As you know congenital CMV infection could be diagnosed by identification of the virus in body fluids before 3 weeks, how could you document the congenital nature of infection in children older than 21 days in your study?

- Table 1: Age at surgery is not compatible with the age of cataract appearance in children, and this categorization may be error-prone.
- Table 2 is confusing, if it is not necessary to show both univariable and multivariable results, you can show only one group of results.
- Discussion: In this sentence" The declining concentration of virus DNA with age suggests that some of the control group had the congenital infection, but confirming this would require assessing the prevalence of HCMV infection in pregnant woman and in their new-borns." The interpretation is questionable because there are many factors for congenital infection in a child. please omit the subheadings.

best wishes

REFEREE: Reviewer | **Revision** (0) 15 Mar 2020

Dear AE,
The study is reviewed carefully. According to comments and revisions by the author, this manuscript is accepted.
Thanks

REFEREE: Associate Editor | **Revision** (0) 15 Mar 2020

Dear EIC
The reviewer(s) have recommended publication, but also suggest some major revisions to the manuscript. Therefore, I invite the author to respond to the reviewer(s)' comments and revise his manuscript.
Kind regards,

REFEREE: EIC | **Revision** (0) 15 Mar 2020

Dear Author,
Thank you for your nice article:
Some point listed which need your attention.
My decision about this manuscript (MAJOR evision).
Thanks

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Reply to Reviewer 1

We thank you for your helpful comments, which we agree, will significantly improve the paper.

We accept the criticism that we cannot be sure that all our CMV and rubella positive cases We accept the central criticism of both reviewers that we cannot be sure that all our CMV and rubella positive cases represented congenital infection, indeed they are much more likely to represent a mixture of congenital and acquired infection. We have now included a 'minimum estimate' of congenital infection of 15/65 (23%) cases who had virus in the lens aspirate on the basis that virus would not get into the lens matter in acquired cases.

Because congenital cataract does not present early in Sub Saharan Africa it is impossible to restrict this kind of study to the age group where congenital infection can be confirmed biologically.

We have discussed this in the paper already (sentences 2,3,4 in paragraph 1 of the discussion and Paragraph 2 of the discussion explains the reasons we feel our results portray a mixed picture of congenital and acquired infection) but have now highlighted this point to make it much clearer and more obvious as follows:

1. In the first sentence of the conclusion of the abstract we have added ' Although most of the children in the study presented too late to be sure that infection was congenital,…'
2. We have added a whole paragraph highlighting this limitation of the study but explaining why we still feel it presents good evidence for the role of congenital infection. This is now the penultimate paragraph of the discussion.
3. We have removed the sentence at the start of the last paragraph of the discussion stating that congenital infection accounts for 51 / 65 cases, changing it to 'is an important cause of…'

Abstract

qPCR - We have now capitalized Quantitative Polymerase Chain Reaction to make this clearer

HCMV – human cytomegalovirus - now spelt out in background of abstract

SSA – sub Saharan Africa – now spelt out in background

Materials and methods

Subheadings have been removed as requested

Matching controls for weight – we can see the merit of this argument but we were interested to investigate birthweight as a possible independent risk factor for infantile cataract in this population and, if we had matched for weight, we would not have been able to investigate and show that it was indeed an independent risk factor.

Results

Regarding children over 3 weeks of age please see above comments

Table 1. Thank you for pointing this out. Although the children were operated on very soon after presentation, it was confusing as it was and we have now changed the heading to age at surgery.

Table 2. Thank you for this comment - we agree and have removed the multivariate analysis

Discussion

The declining concentration of virus DNA with age suggests that some of the control group had congenital infection….we have removed the second half of this sentence as requested.

Reply to Reviewer 2

We accept the central criticism of both reviewers that we cannot be sure that all our CMV and rubella positive cases represented congenital infection, indeed they are much more likely to represent a mixture of congenital and acquired infection. We have now included a 'minimum estimate' of congenital infection of 15/65 (23%) cases who had virus in the lens aspirate on the basis that virus would not get into the lens matter in acquired cases.

Because congenital cataract does not present early in Sub Saharan Africa it is impossible to restrict this kind of study to the age group where congenital infection can be confirmed biologically.

We have discussed this in the paper already (sentences 2,3,4 in paragraph 1 of the discussion and Paragraph 2 of the discussion explains the reasons we feel our results portray a mixed picture of congenital and acquired infection) but have now highlighted this point to make it much clearer and more obvious as follows:

1. In the first sentence of the conclusion of the abstract we have added ' Although most of the children in the study presented too late to be sure that infection was congenital,…'
2. We have added a whole paragraph highlighting this limitation of the study but explaining why we still feel it presents good evidence for the role of congenital infection. This is now the penultimate paragraph of the discussion.
3. We have removed the sentence at the start of the last paragraph of the discussion stating that congenital infection accounts for 51 / 65 cases, changing it to 'is an important cause of…'

Another query is about congenital versus acquired infection, which we have addressed at length above

The second query is this:

In your research, both rubella and CMV were searched by laboratory findings. how can you specify the exact microbial causes of eye problem, which one? Rubella or CMV? Please explain that.

Thank you for seeking clarification here. We have added 2 paragraphs (para 4 and 5 in the results) to give greater clarity about which patients had HCMV, rubella and both.

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Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (1) 27 Apr 2020

Dear AE,
Thanks for the revision, there are a few notes:
- Totally since the study population is less than 12 months so the diagnosis of congenital cataract is difficult, but lens infection can be more prevalent in congenital cases of rubella. Concerning high prevalence of postnatal infection in CMV cases, the results are more prone to bias.
1- Please move ethical consideration to the end of methods.
2- If you have ethical code plz give it.
3- What was the characteristics of control subjects, from what population were they selected, Were the case and control groups matched for age and other confounding variables?
4- Plz give P-value in table 1, on your data on age and HCMV.
Best thanks

REFEREE: Associate Editor | **Revision** (1) 2 May 2020

Dear EIC,
Thanks for the authors' attention to our comments. Please revise it and submit again based on the comments of reviewers.
Best regard

REFEREE: EIC | **Revision** (1) 2 May 2020

Dear Author,
My decision about this manuscript is Minor Revision.
Thanks

OPEN PEER REVIEW

Revision (2)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Reply to Reviewer

We thank you for your helpful comments, which will further improve our paper.

1. We have moved ethical consideration to the end of methods.
2. Ethical numbers/code have been provided.
3. Regarding control subjects, we have described the characteristics of control subjects (sentence 1,2,3&4 in paragraph 2 of methods) as follows:
   Controls were children less than 12 months of age without cataract or obvious ocular pathology and/or any other systemic problems. They were selected from population of children less than 5 years of age attending reproductive and child health clinics for routine immunizations and nutrition check. Case and control groups were all age matched. They were not matched for weight since we were interested to investigate birthweight as a possible independent risk factor for infantile cataract in this population and, if we had matched for weight, we would not have been able to investigate and show that it was indeed an independent risk factor.
4. P-value in table1: Age at surgery vs. HCMV in saliva, lens and DBS have now been provided.

OPEN PEER REVIEW

Revision (2)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (2) 16 May 2020

Dear AE,
The study is reviewed carefully. According to comments and revisions by the author, this manuscript is accepted.
Thanks

REFEREE: Associate Editor | **Revision** (2) 17 May 2020

Dear EIC
Based on the authors' answers to the reviewers' comments, the reviewer(s) have recommended publication.
Kind regards.

REFEREE: EIC | **Revision** (2) 18 May 2020

Dear Author,
The document is reviewed carefully by the reviewers. According to their comments and your revisions as requested, this manuscript is accepted.
Thanks.