

## PEER REVIEW HISTORY

BMJ Paediatrics Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Neurodevelopmental Delay in Normocephalic Children with in utero Exposure to Zika Virus
<b>AUTHORS</b>	Faical, Adriana; de Oliveira, Juliana; Oliveira, João Vitor; de Almeida, Breno; Agra, Iluska; Alcantara, Luiz Carlos; Acosta, Angelina; de Siqueira, Isadora

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Reviewer name: Joao Guilherme Bezerra Alves Institution and Country: Instituto de Medicina Integral Prof. Fernando Figueira (IMIP), Brazil Competing interests: I declare no competing interests
<b>REVIEW RETURNED</b>	13-May-2019

<b>GENERAL COMMENTS</b>	<p>The work is well written and presented, as well as addressing a topic of importance.</p> <p>However some issues deserve better clarification:</p> <p>1 - More details about congenital Zika infection are needed especially because the reference 4 which describes the recruitment of children is only an abstract: serological tests (IgG or IGM or both); both tests in children and mother?; how many children or mothers had PCR?;</p> <p>2 - What this phrase means? "The present study did not include patient or public involvement". (line 93)</p> <p>3 - How prematurity was conducted regarding Bailey III? How many children with neurodevelopment delay were preterm?</p> <p>4 - Audiological evaluations were performed in all children with language delay?</p> <p>5 - Did any of these children undergo neuroimaging?</p>
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<b>REVIEWER</b>	Reviewer name: Isis Nem De Oliveira Souza Institution and Country: Federal University of Rio de Janeiro, Brazil Competing interests: I declare no competing interests.
<b>REVIEW RETURNED</b>	21-May-2019

<b>GENERAL COMMENTS</b>	<p>In this study, Faical and colleagues evaluated neurodevelopment in a cohort of normocephalic Zika virus-exposed children. The rationale for the study was clearly stated at the initial paragraphs; the chosen method was well explained; the results were easily understandable and the discussion fit for the data. I recommend the citation of "Description of 13 Infants Born During October 2015–January 2016 With Congenital Zika Virus Infection Without Microcephaly at Birth — Brazil" by Van der Linden et al., 2016, as this paper supports the neurodevelopmental deficits found in normocephalic Zika-infected infants in the Northeast of Brazil, enriching both the rationale and the discussion of the manuscript.</p>
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	Apart from this minor recommendation, the work represents a considerable contribution to the field and therefore, I recommend the manuscript for publication in its present form.
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# **VERSION 1 – AUTHOR RESPONSE**

Reviewer #1:

The work is well written and presented, as well as addressing a topic of importance.

However some issues deserve better clarification:

1 - More details about congenital Zika infection are needed especially because the reference 4 which describes the recruitment of children is only an abstract: serological tests (IgG or IGM or both); both tests in children and mother?; how many children or mothers had PCR?;

We agree with the reviewer suggestion and we added the information requested on lines 77-78.

2 - What this phrase means? "The present study did not include patient or public involvement". (line 93)

This statement was a request from BMJ Pediatrics Open.

"BMJ encourages active patient and public involvement in clinical research as part of its patient and public partnership strategy. To support co-production of research we request that authors provide a Patient and Public Involvement statement in the methods section of their papers"

[https://bmjpaedsopen.bmj.com/pages/authors/#reporting\\_patient\\_and\\_public\\_involvement\\_in\\_research](https://bmjpaedsopen.bmj.com/pages/authors/#reporting_patient_and_public_involvement_in_research)

3 - How prematurity was conducted regarding Bailey III? How many children with neurodevelopment delay were preterm?

The Bayley-III allow an adjustment for prematurity in calculating the child's age at the time of testing. The adjustment was done regarding the number of months and days of prematurity, to determine the appropriate start point. We added a statement on lines 84-85.

Three infants with neurodevelopment delay were preterm and two infants without delay, with no difference between both groups ( $p=0.68$ ).

4 - Audiological evaluations were performed in all children with language delay?

No. Audiological evaluations were performed in 16 (55.1%) infants, including five out of nine of the infants with language delay. We added this information on line 127.

All the infants were forwarded to Audiological evaluations, however 13 didn't show up for the evaluations.

5 - Did any of these children undergo neuroimaging?

No neuroimaging was performed. We added this statement on line 97.

Reviewer #2:

In this study, Faiçal and colleagues evaluated neurodevelopment in a cohort of normocephalic Zika virus-exposed children. The rationale for the study was clearly stated at the initial paragraphs; the chosen method was well explained; the results were easily understandable and the discussion fit for the data. I recommend the citation of "Description of 13 Infants Born During October 2015–January

2016 With Congenital Zika Virus Infection Without Microcephaly at Birth — Brazil" by Van der Linden et al., 2016, as this paper supports the neurodevelopmental deficits found in normocephalic Zika-infected infants in the Northeast of Brazil, enriching both the rationale and the discussion of the manuscript. Apart from this minor recommendation, the work represents a considerable contribution to the field and therefore, I recommend the manuscript for publication in its present form.

We thank the reviewer for the comments and the useful suggestion to improve our manuscript. We added a comment on lines 67-68 and updated the reference list.