Author’s response to reviews

Title: Seroprevalence of dengue IgG antibodies in symptomatic and asymptomatic individuals three years after an outbreak in Zhejiang Province, China

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Author’s response to reviews:

Dear Editors and Reviewers,

Thank you for your comments on our manuscript entitled “Seroprevalence of dengue IgG antibodies among patients and asymptomatic individuals three years after infection during an outbreak in Zhejiang Province, China” (INFD-D-17-01171). Those comments are all valuable and very helpful for improving our paper. We have studied comments carefully and have made correction which we hope meet with approval. Moreover, we invited an English native speaker to revise the manuscript. All the contributing authors have reviewed the revision and concur in the revised submission.

Respond to Reviewer 1:

1. Respond to comment: The number of samples analysed is rather low. Therefore it is a pity that the quantity of Dengue specific IgGs could not be analysed due to the missing quantitative results. It would be interesting to know how much the antibody titre decreases within the 3 years. This is a significant limitation of the study.
Response: In 2009, dengue RNA or IgM was detected in the serum specimens of patients and asymptomatic individuals. In 2012, dengue IgG was detected in samples from those people. It is a pity that dengue IgG was not detected in 2009. Therefore, we are very sorry that we can’t know how much the antibody titre decreases within the 3 years. We add this limitation in the discussion section.

2. Respond to comment: For the following statement please provide the references of the previous reports or delete the sentence. "According to previous reports, the existence of dengue antibodies could enhance dengue infection and zika infection."

Response: We add 7 references.

3. Respond to comment: This description is part of the Dengue sample characterisation and should be in M&M. "No dengue outbreak occurred from 2009 to 2012 in Zhejiang Province, and all patients and asymptomatic individuals hadn't traveled to dengue endemic areas during these years."

Response: We removed this sentence to M&M.

4. Respond to comment: The study describes several limitations but listed just three. However there are some more lessons to learn how to improve such seroprevalence studies. There should be also a verification of the PanBio ELISA results by other serological assays

Response: We revised limitation section. These limitations suggested that antibodies and antibody titres should be detected in every year to explore antibody dynamics in such seroprevalence studies. We are sorry that we didn’t verify the PanBio ELISA results by other serological assays due to limited funds. PanBio company provided sensitivity and specificity of their assays.

Thank you again for your valuable comments.

Respond to Reviewer 2:

1. Respond to comment: The selection of samples were not clearly described and the conclusion were based on a small sample especially assessing seroprevalance.

Response: We revised relative sentences. In 2009, an outbreak of DENV-3 subtype III occurred in Yiwu, a central city of Zhejiang Province in Southeastern China and a total of 196 cases were identified in this outbreak [19]. An acutely ill person with acute onset of rash, headache, subjective fever, itching, anorexia, or arthralgia and dengue RNA or IgM was detected in his serum specimen was defined as a dengue confirmed case. After this outbreak we conducted an investigation of asymptomatic infection and 102 asymptomatic individuals were identified.
during the outbreak [20]. A person with no symptoms and dengue IgM was detected in his serum specimen was defined as an asymptomatic individual. In 2012, we collected blood samples from 59 dengue cases patients and 48 asymptomatic individuals who agreed with the informed consent.

2. Respond to comment: The sample collection setting need further description like endemicity and the possible cocirculation of other flaviviruses which might have an impact on the assay used.

Response: We added some sentences. No dengue outbreak occurred from 2009 to 2012 in Zhejiang Province, and all patients and asymptomatic individuals in our study hadn’t traveled to dengue endemic areas during these years. Moreover, only one Japanese Encephalitis case were reported from 2004 to 2012 and no other flaviviruses were endemic in these villages where our samples were collected.

3. Respond to comment: Do the authors have attempted to identify the serotype in the samples collected. Although the endemic was due to DEN III serotype 3, have the authors made an attempt to identify other serotypes in the study population which might contribute to the seropositivity.

Response: Dengue is not endemic in Zhejiang Province, China and all outbreaks were triggered by imported cases. In the outbreak of 2009, all cases were infected with DENV serotype 3. In 2012, only dengue IgG antibodies were detected and it was impossible to identify DENV serotypes.

4. Respond to comment: There is no reference to weather the infection is primary or secondary and it would be interesting to assess the weaning of antibody response in relation to primary Vs secondary and in relation to different serotypes.

Response: Dengue is not endemic in Zhejiang Province, China and all outbreaks were triggered by imported cases. It is the first dengue outbreak in Yiwu City in 2009. The infection is primary.

We have tried our best to improve the manuscript and made some changes in the manuscript. We appreciate for Editors/Reviewers’ warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.

Yours sincerely,

Jimin Sun