Reviewer's report

Title: Cross-sectional study of cytomegalovirus shedding and immunological markers among seropositive children and their mothers: potential implications for viral transmission

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Reviewer: Sophie Alain

Reviewer's report:

Comments:

This a quite interesting and clever study, though with very low numbers of participants. As there are many studies describing the prevalence of CMV excretion in urines and saliva, especially in the US, within various classes of age, the study is not very original. The main interest is probably to describe the distribution of viral loads in the population per age and thus to better identify the risk per class of age. This link could be enhanced by the follow-up announced as a companion study, and whole results presented together would probably be much more informative and original, because follow-up study are not available in this population.

The study has some pitfalls well underlined and discussed by the authors. The sample size, that make the results significant only as “trends”, especially for high viral loads risk factors identification is, to our opinion, the only problem. The other points are minor and well discussed by the authors.

The authors mentioned the disparity of sampling methods which impairs comparison of urine and saliva viral loads. (The comparison between urine and saliva by qualitative methods has yet been published). This is true but we underline that direct sampling of urine from children is quite impossible, and so the authors did their best. One way to enhance the comparison could have been to report CMV copies per ng of extracted total nucleic acids from both saliva and urines.

They also underlined the fact that infectious CMV cannot be assessed by PCR in saliva. We agree with that but the higher viral loads are very likely to be associated with the presence of infectious virus (shown by previous studies of virus detection in urines).

Another possible bias is the recruitment within the local population probably not representative of the whole population (may be due to the way of recruitment?) (high rates of breast milk feeding, socioeconomic conditions, day-car center, are factors collected by the authors and that could have largely influenced the CMV transmission and thus, the prevalence of primary infections in children, but may not reach significance in this small population). However, we can consider that this is a descriptive study from a small special population, and here again, the
study will be largely enhanced by the companion paper’s results to see how the virus spreads in the population.

To this purpose the link between the detection of low-avidity anti-CMV antibody and excretion is interesting and reflect the route of acquisition of CMV in young children.

The last point is that the excretion prevalence is very high (100% but 8/8) in the >12 months children population, compared to some previous studies using PCR in saliva, suggesting a recruitment bias towards a high-risk population. This is in agreement with the high prevalence of excretion in mothers showing that CMV circulates actively in this population. This last point, could be interesting to discuss in this paper.

Finally, this study is interesting and will benefit from comparison with the follow up analysis. It could be therefore be published now as a cross-sectional study and followed by a longitudinal study more interesting in terms of routes and consequences of CMV circulation in the population.

- Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)
  
  Figure 1 in which the categories are only based on the authors assumption of the route of transmission is quite subjective, though illustrative. May be withdrawn?

- Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

- Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)

The study is probably too preliminary to be published as a full length paper. It could better be presented as a short preliminary study (or feasibility?) before a longitudinal study of CMV transmission in population.

Though the viral load measurements are interesting, the small size of the population does not allow to generalize the conclusions to other populations and the authors should be very cautious before counselling on such preliminary results.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I do not consider that we have competing interests, however I have to declare that
we had completed two studies on viral load in saliva from toddlers together with culture, the first in emergency unit population and the second in a large national level population of 1650 children from day-care centers. However, the design of the study is very different, as we did not aimed to measure the antibody level in serum neither from toddlers, nor from mothers but better to study the risk factors for CMV transmission, and we did not organized longitudinal follow-up. So we consider that there is no competition between the studies.