Reviewer’s report

Title: Prevalence of Noroviruses in Children Hospitalized for Acute Gastroenteritis in Hohhot, China, 2012–2017

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Reviewer: David Allen

Reviewer's report:

Li et al present a study of norovirus-associated gastroenteritis among hospitalised children under 5 years of age in Hohhot, China. The authors find norovirus associated with around one quarter of acute gastroenteritis cases in the population studied, and present data on the molecular epidemiology of the virus, demonstrating GII.3 to be the most commonly detected genotype overall, and show that GII.4 genotype viruses were associated with at least two polymerase types.

This study contributes to understanding the epidemiology of norovirus infections in infants, and adds to the knowledge base on the global surveillance of norovirus types circulating worldwide.

1. The manuscript requires proof-reading for grammatical accuracy and clarity of English to meet the standard of the journal.

2. The use of the terms describing PCR-based methods must be clarified throughout: the abbreviation "RT-PCR" is more correctly used to describe reverse-transcription PCR (as opposed to real-time PCR as used here), which the authors use for both meanings (se Line 24 cf. Line 102).

3. Line 100 - the authors should clarify their methodology, as they do not make clear reference to any reverse transcription process, either as a one-step real-time RT-PCR, or real-time PCR preceded by separate cDNA synthesis.

4. Line 102-103 - the phrase "RT-PCR for genotyping sequence" does not make sense, and should be rephrased for technical accuracy to describe the method used.

5. Line 110 - the phrase "amplicons of the partial sequences" does not make sense and should be rephrased for technical accuracy.

6. The authors present statistical test data for a number of observations (Lines 131-135) for which they show no statistical significance; however, the authors proceed to indicate an important difference between age groups 0-23 and 24-48 months, but do not support the observation with statistical testing. The authors should provide statistical analyses consistently throughout the manuscript.
7. Line 145 - it is not clear whether the 450 norovirus-positive samples referred to are only genogroup II or account for both genogroup I and II. The information provided in the methods suggests (although is not clear) that both genogroup I- and II-specific testing was performed, but the detection data for each genogroup is not clearly presented.

8. Line 161 - do the authors mean during the year 2012 and the year 2017, or across the six year period 2012-2017?

9. Line 163-164 - did the authors find a statistical significance in the age difference between GII.3 vs GII.4 infections?

10. Line 169-170 - the authors should clarify their observations on the epidemiology of GII.3 strains. It is not clear from Figure 4 which year are epidemic years - and use of the term "alternate" here implies year-to-year switching between the two strains, which from the data presented in Figure 4, is not the case.

11. Line 180-182: the authors make reference to different GII.4 capsid types detected, for which: (1) the authors should provide specific reference (paper citation and/or accession number) of the strain to which the comparison was made, and (2) clarify if the information regarding the New Orleans strain is correct: the global dominant strain would be the GII.4/2009 virus, although the authors refer to a 2010 virus in the text.

12. The authors should establish a clear and consistent nomenclature for referring to virus types and strains, e.g. the authors refer to "Sydney 2012", "GII.4/Sydney" and "GII.4/Sydney 2012" at different points in the manuscript; these and similar naming terms should be unified into a single approach that is also consistent with terminology used in the wider literature.

13. Figure 3 - it would be useful to annotate the figure with the numerators for each bar, and in the legend specifically provide the relevant denominator figures, from which percentage data were generated.

14. Figure 4 - with the analysis and commentary provided on polymerase-capsid recombination in the manuscript, it would be useful to see both polymerase and capsid data represented in this figure, either combined or as two separate panels.

15. Figure 5 - it is difficult to identify the sequences from the study in the tree provided. There are no obvious labels that indicate accession numbers MK319151-MK319216. Also, with much emphasis in the analysis on GII.3 viruses, it is unclear why the authors have chosen to collapse these branches, losing resolution in their data on these sequences. The legend to the figure does not make clear what the filled triangles represent in the tree.

16. There is a distinct sampling bias between infants <24 months of age and those >24 months of age: does the largely different denominator in these two populations affect the significance of the authors' observation that the rate and type of norovirus infection differs before/after 24 months of age (see also comment #6)?
17. The authors discuss factors that may explain their observations, such as local climate - which would be strengthened if there were some meteorological data that could be included in their analyses. Further, can the authors comment on other drives that might have influenced the observations, such as risk factors and healthcare-seeking behaviour among the population studied, and any differences in these factors within (e.g. younger vs older children).

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**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

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I recommend additional statistical review

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