Author’s response to reviews

Title: Burden of rotavirus gastroenteritis in the Middle Eastern and North African pediatric population

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Author’s response to reviews: see over
Dr Xuzhuang Shen  
Associate Editor  
BMC Infectious Diseases  
bmcserieseditor@biomedcentral.com

Dear Dr Shen,

Re: Burden of rotavirus gastroenteritis in the Middle Eastern and North African pediatric population  
Hanane Khoury, Isla Ogilvie, Antoine C. El Khoury, Yinghui Duan, Mireille M. Goetghebeur

We would like to thank the reviewers for their comments, which were considered in revising the attached manuscript. We gathered from the reviewers’ and the editor’s comments that the methodology did not adhere to the PRISMA guidelines; therefore we identified the manuscript as a “comprehensive” rather than “systematic” review, and edited the text accordingly. The text was also revised to respond to specific comments from the reviewers. Please see below detailed responses to each comment. We also changed the colors and shading in the graphs for more clarity.

We hope that these modifications make this manuscript suitable for publication in BMC Infectious Diseases.

Sincerely yours,

[Signature]

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Detailed response to reviewers

Reviewer 1

- The authors propose a systematic literature (RS) review on the burden of rotavirus acute gastroenteritis on the paediatric population in two wide regions of the Earth (Middle Eastern and North African). The information worked out from these types of study are too much heterogeneous in aims, methods and population characteristics. Hence comparing two or more studies on systematic literature become too difficult. Moreover the validation of a RS and the accuracy of its results depend to the precision applied in phase of construction of the experimental design. The evaluation of the methodological quality of the epidemiological studies in an RS is a fundamental aspect to give into account in order to avoid the BIAS and to get a correct interpretation of the results: in this work this assessment was not specified.

Reply: This review did not include any qualitative assessment of the design or results of the studies included; therefore it is now identified as a comprehensive rather than a systematic review.

- The authors didn’t emphasized the strategies used (if used!!) for resuming the information and the criteria adopted for the choose of one reference instead of another. Finally the authors didn’t specified clearly the aims of the paper: for example it is not clear if the review is referred also to the spatial-temporal distribution of circulating Rotavirus genotypes.

Reply: all articles containing relevant data were included in this review. Exclusion criteria were limited to reviews and case reports; this is now specified in the materials and methods section. In one case (Ceyhan et al., Turkey), discrepancies in genotype reporting were found that resulted in the exclusion of this study from the genotype sections; this is reported under Data Extraction and Analysis section (3rd paragraph). The strategy for extracting and summarizing data is described in the materials and methods (data extraction and analysis section); for example: “For healthcare resource utilization data, the following parameters were extracted for comparison across countries: hospital admission rates, need for intravenous rehydration, and duration of hospital stay. Cost-of-illness data included direct medical costs, out-of-pocket expenditures,...”

- Introduction: It would be useful to add some information about the vaccine used for the prevention of Gastroenteritis caused by Rotaviruses.

Reply: the following information was added to the introduction: “...Currently available rotavirus vaccines protected against severe RVGE and were well tolerated; the implementation of immunization programs would be expected to reduce disease burden.”

- Materials and methods: The Tests of statistical analysis used must be indicated in this section.

Reply: given the qualitative purpose of this review, no statistical analyses were conducted. This information was added to the data extraction and analysis section as follows: “No statistical analyses were performed for this review”.

- Discussion: In page 14 line 18 the authors could specify that the G12 strain was isolated even in Europe, specifically in Italy (see reference: G genotyping of rotaviruses in stool samples in Salento, Italy, Grassi T. et al 2006 J Prev Med Hyg).

Reply: the discussion text was revised and Grassi’s publication cited as follows: “Interestingly, G12, a recently emerging serotype detected in Europe, Asia, and the Americas,[11,60,61] has not been reported in any of the studies captured in this review.”
Reviewer 2

• Methods: Were reviews excluded from the analysis? If not, how did the authors account for potentially duplicate data?

Reply: reviews were excluded in this study, as indicated now in the materials and methods section.

• Methods: Why were the publications selected limited only to those published between 1999-2009, especially since date of study rather than publication was used in the analysis?

Reply: this timeframe was chosen to gather the most recent data available on the burden of RVGE.

• Methods: Was consideration give to including the term “hospitalization” or “outpatient” in the search criteria?

Reply: although these terms were not included in the search algorithm, data relevant to hospitalization and medical care sought was extracted whenever available.

• If possible, it would be easier to interpret data if medians were reported if available, rather than means or averages.

Reply: we agree with the reviewer on the informative power of medians; however, for many countries, data was available from one source only and was reported as originally described in the source document. Therefore, pooled averages for certain countries were selected to compare to the original figures.

• Results: It would be useful to present a summary of the 44 papers by country or region within the Middle East or North Africa.

Reply: a table (Table 1) summarizing literature capture and data sources by country was added to the results; the text was revised accordingly.

• Results: If possible, data regarding breakdown between hospitalizations and outpatient visits or non-medically attended visits should be reported.

Reply: Hospitalization data is reported as part of Healthcare Resource Utilization in the results section. Data for outpatient visits or non-medically attended visits was limited to one study, therefore we decided not to include this data in the manuscript.

• Results Pg. 8: Why do the authors postulate that the rotavirus prevalence rates changed so dramatically in Egypt and Iran (increased) and Saudi Arabia (decreased)? Were there differences in the studies that were conducted or was there evidence to suggest why these major shifts occurred in the publications?

Reply: the text here refers to a descriptive rather than quantitative comparison of prevalence rates for a given country. No information was available to estimate the epidemiological trends in RVGE across countries.
• Discussion: Would it be possible for the authors to extrapolate the data they have reviewed to an estimate of actual numbers of infants with rotavirus gastroenteritis, hospitalization, outpatient visits, and deaths by age group (for instance < 6 months, 6-12 months, 12-24 months, 2-5 years) in the region as a whole?

Reply: data by age group was not reported in all studies included in this review, and whenever reported, age stratification varied between studies, thereby making data extrapolation not feasible.

Associate editor's comments

• In data extraction and analysis, authors should simply explain Vesikari scoring.

Reply: this section was edited to include the following sentence: “...The Vesikari scale is a numerical system used to assess RVGE disease severity,...”

• The part of materials in the study, there is too much and complex, hence some of the presentation is ambiguous, for example the content of the genotype can be less and more clear.

Reply: the genotype data extraction and analysis was revised as follows to clarify: “Data was extracted for each serotype. Figures for distribution of rotavirus genotype combinations were taken from the most recent available data, except for Turkey. For this country, data from a prospective survey from 2004–2005[14] was used to replace a more recent publication (2005-2006 Ceyhan study[15]), due to discrepancies in the serotype data reporting (combined serotyped data in the Ceyhan study[15] adds up to 113%).”

• Also, in the discussion, the data from result could not be listed again.

Reply: the discussion text was revised to avoid repetition of data presented in the results section.

• Because of the data limitation, the authors could not tell the relationship of the genotype the severity of the disease, which is a deficiency.

Reply: the following text was added to the study limitations’ paragraph in the discussion: “…Moreover, due to data limitations, a clear relationship between certain rotavirus genotypes and disease severity could not be established…”

• Editorial Requests: Please can you adhere to the PRISMA guidelines http://www.prisma-statement.org/.

Reply: we revised Figure 1 (Flowchart of study selection) to reflect a typical Prisma flow diagram. Also, as mentioned previously, since this review did not include any qualitative assessment of the design or results of the studies included, it is now identified as a comprehensive rather than a systematic review.