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Manuscript Type: REVIEW

Response to reviewers

Reviewer 1:

We added a figure displaying the known data on HDV prevalence and the most frequent clades. Also the corresponding text was added in the introduction section

A conclusion section was added in the end of the manuscript. Future research trends are specifically referred in this section as well as throughout the text.

We decided not incorporating a table detailing out available treatment modalities since, as we refer in the text, the only options are interferon or PEG-interferon. Both are not specific but are the only approved in AASL and EASL guidelines for treatment. The same information can also be obtained in www.who.org.

A few molecular epidemiology aspects are now incorporated in the introduction section. This specific issue, being of course important, is not a main subject of this review.

Reviewer 2:

Specific data about HDV epidemiology and outcomes in children are very scarce in literature. The few available studies suggest the same genotype distribution as in adults and a probable similar response to standard treatments. These studies include a very limited number of patients (reviewed in Xue MM, Glenn JS, Leung DH.J *Pediatr Gastroenterol Nutr.* 2015 May 20) and we don't believe that highlighting children as a separate group of patients would make these issues clearer for the reader.

As for Reviewer 1, we included a map displaying data on HDV prevalence and the most frequent clades.

Reviewer 3

English was checked throughout the manuscript and corrected according to the reviewer's comments.

Concerning the "Origin of the virus section" we believe that it would be clearer, and perhaps more logical, for the reader to keep it in the end. There is a considerable amount of questions that remain to be answered regarding the origin of HDV. Examples include the details of virus RNA replication by a host enzyme, the rod-like structure of the genome, the origin of the Delta antigen, etc, etc. Discussing the origin of the virus in the beginning of the manuscript will be difficult since the reader is still not introduced to fundamental aspects of virus structure and replication strategy. We ask you to consider the possibility of keeping this section in the end.

Yours sincerely,

Celso Cunha