



## ANSWERING REVIEWERS

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Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 5751-review.docx).

**Title:** HEPATITIS C VIRUS GENOTYPE 6: Virology, Epidemiology, Genetic variation and Clinical implication

**Author:** Vo Duy Thong, Srunthron Akkarathamrongsin, Kittiyod Poovorawan, Pisit Tangkijvanich, Yong Poovorawan.

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 5751

The manuscript has been improved according to the suggestions of reviewers:

1. Format has been updated
2. Revision has been made according to the suggestions of the reviewer
3. References and typesetting were corrected

Please also find attached the itemized responses to reviewers' comments. The authors appreciate the constructive comments and have attempted to modify the manuscript as requested.

We hope that the revised manuscript is now acceptable for publication in the "*World Journal of Gastroenterology*"

Sincerely yours,

Prof. Yong Poovorawan, M.D.

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Reviewer comments (01806390)

## SPECIFIC COMMENTS

1. The introduction is too long and poorly defines aims and scope of this review paper.

Response:

Thank you very much for your suggestion. We have revised and shortened the introduction part. However, we reorganized the text by moving “worldwide HCV genotypes distribution” from epidemiology section to the introduction.

2. No mention is made to the strategy of bibliographic research followed.

Response:

Thank you very much for your comment. We retrieved and selected the related topics on virology, epidemiology, genetic variation and clinical implication of HCV-6 from PubMed database.

3. The manuscript fails to define when HCV in general is being discussed and when specific mention is made to genotype 6 throughout the manuscript and particularly in the section on clinical manifestations, which needs to be shortened to a substantial extent.

Response:

We reorganized and moved HCV in general to introduction part and the scope on HCV genotype 6 in epidemiology and clinical manifestations. Only one published study reported that patients with HCV-6 appear to present with similar clinical manifestations as those with genotype 1 or 2/3, and found that people with HCV genotype 1 and 6 had a somewhat higher baseline viral load than those with others genotypes.

4. Submission 2013 – 0924161038 displays a certain degree of redundancy, which needs to be corrected. For instance, the introduction states that “HCV genotype 1 (HCV-1) is distributed worldwide while HCV-2 and HCV-3 are found commonly in East Asia. HCV genotype 4 and 5 are commonly found in North and South Africa, respectively, and HCV-6 is mainly found in and around Southeast Asia.” And the section on the epidemiology substantially repeats the same concepts “HCV-1 is found commonly worldwide and especially in developed regions such as America and Europe. HCV-2 has high prevalence in Central and West Africa as well as some western countries while HCV-3 is predominantly found in Far Eastern countries and the Indian subcontinent. Meanwhile, HCV genotypes 4, 5 and 6 are endemic to specific geographical areas:

HCV-4 is mainly found in Egypt and Sub-Saharan Africa, HCV-5 has accumulated in South Africa, and HCV-6 is most common in South China and South East Asian countries". Similarly, the statement that HCV (genotype 6) is chiefly transmitted via the intravenous drug use does not need to be duplicated through the manuscript.

**Response:**

We removed and revised the redundancy.

5. No mention is made to the interaction, if any, between HCV genotype 6 and host metabolic features, notably including steatosis. A short paragraph needs to be added on this, given that steatosis is a chief modulator of clinical course of HCV infection (Adinolfi LE, Expert OpinPharmacother. 2011;12:2215-34.) and that Asians appear to be prone to the development of metabolic disorders at lower values of body mass index and waist circumference compared to other ethnicities.

**Response:**

We mention this content (Adinolfi LE, Expert OpinPharmacother. 2011;12:2215-34.) in the text in the clinical section. However, there appears to be no published data specific to genotype 6.

6. Are there any data available on HIV-HCV GT 6 or HBV- HCV GT 6 co-infection ?

**Response:**

We cannot find any data mentioning HIV-HCV GT6 or HBV-HCV GT6 co-infection

7. Add a short paragraph specifically highlighting findings from studies on HCV genotype 6 performed in non-Asian countries.

**Response:**

HCV-6 is most common in South China and South East Asian countries. Some studies on HCV genotype 6 performed in U.S. and Canada Asian immigrants were added to Epidemiology and Treatment part.

8. Table 1 fails to report the number of subjects evaluated in each study. Moreover, I would suggest putting together Author, year and Reference in the same column.

**Response:**

In Table 1, we used data collected from our research and from high prevalence of HCV-6 among Asian population. We thought that putting together Author, Year and Reference in the same column may be confusing. We have arranged to make Table 1 clearer.

9. Additional original tables are needed to summarize chief findings from the few available studies on HCV genotype 6.

**Response:**

We reported some findings from available studies on HCV-6 in Table 1 and Figure 5.

10. In Figure 1 Germany and France have seemingly been located in Africa. Australia has a spelling mistake.

**Response:**

We apologized for the mistakes and have made the corrections.

11. The manuscript is incompletely referenced and all the following need to be quoted and discussed where appropriate: M. Michele Manos, *Journal of Medical Virology* 2012; 84:1744–1750 ; SubhashMedhi *Arch Virol* 2012; 157:2083–2093; Nguyen LH *Aliment PharmacolTher* 2013; 37: 921–936; Seong Clin *Mol Hepatol* 2013;19:45-50; ChalermratBunchorntavakul, *World J Hepatol* 2013 ; 5: 496-504; Wantuck JM, Ahmed A, Nguyen MH. *Aliment PharmacolTher*. 2013 Nov 19. doi: 10.1111/apt.12551.

**Response:**

We added three related HCV-6 references (M. Michele Manos, *Journal of Medical Virology* 2012; 84:1744–1750; SubhashMedhi *Arch Virol* 2012; 157:2083–2093; SeongClinMolHepatol 2013;19:45-50) in red track changes of the manuscript. However, the references (Nguyen LH *Aliment PharmacolTher* 2013; 37: 921–936; ChalermratBunchorntavakul, *World J Hepatol* 2013 ; 5: 496-504; Wantuck JM, Ahmed A, Nguyen MH. *Aliment PharmacolTher*. 2013 Nov 19. doi: 10.1111/apt.12551) do not relate to HCV-6, therefore we did not include those in our manuscript.