

June 10, 2018

Dear Dr. Ze-Mao Gong

All authors would like to thank you for your interest in our study titled: “Systematic Overview of Hepatitis C Infection in the Middle East and North Africa”; and for allowing us to respond to the comments raised by the reviewers.

All authors would also like to sincerely thank the reviewers for the review of our manuscript and their thoughtful comments.

Please find attached a revised the manuscript and a point-to point response to each of the reviewer’s comments.

Yours sincerely,

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Point-to point response to reviewers

Name of journal: World Journal of Gastroenterology

Manuscript NO.: 36844

Column: Systematic Review

Title: Systematic Overview of Hepatitis C Infection in the Middle East and North Africa

Authors: Karima Chaabna, Sohaila Cheema, Amit Abraham, Hekmat Alrouh, Albert B Lowenfels, Patrick Maisonneuve, and Ravinder Mamtani

Reviewer reports:

Reviewer #1:

Chaabna et al. extensively reviewed Hepatitis C Infection in the Middle East and North Africa. But their focus is not clear. Authors should make shorten of their manuscript.

Response: We would like to thank Reviewer #1 for this comment. Our overview of systematic review is a scoping review, which includes all relevant data related to the epidemiology of hepatitis C infection in the Middle East and North Africa (MENA) region. The manuscript has been revised to be focused on the primary objective of our overview, which is to assess the quality of the data reported by the published systematic reviews of HCV epidemiology in MENA countries taking into account conflict of interest disclosed by the authors of these SRs (Introduction section, page 7). As suggested by the reviewer, we have now shortened our manuscript. Two tables have been created in the supplementary materials to sum up the data previously reported in the manuscript text that was related to our secondary objective, which is to produce a comprehensive picture of hepatitis C infection epidemiology in the 20 countries of the MENA region.

1 In abstract section, "The extracted outcomes were HCV antibody (anti-) prevalences and incidences in different at-risk populations; the HCV viremic (RNA positive) rate in HCV-positive individuals;... " is unclear.

Response: We have now clarified the primary outcomes of interest as suggested by the reviewer (Abstract, page 3).

2. In page 9, line 15, what is "HsAg"?

Response: We meant *HBsAg* (hepatitis B surface antigen). To clarify, this has now been included in the manuscript text (Materials and Methods section, Primary outcomes subsection, page 9).

3. Authors should make one figure of MAP of MENA regions. Why does Pakistan have HCV GT3? They should more discuss.

Response: We would like to thank the reviewer for this relevant suggestion. We have now included a map of the MENA region (Figure 2).

Robaeys, 2016 in Journal of Hepatology explained that hepatitis C genotype 3 is specific to the hepatitis C virus transmitted through injecting drug use. Hence, in Pakistan, intravenous drug use is likely to be one of the main reasons why hepatitis C genotype 3 is the most common in the country. We now further discuss the predominance of genotype 3 in Pakistan by citing Omata 2015, which reported the emergence of genotype 3 in Pakistan since the 1920s (Discussion section, page 34).

4. Please refer the following reference: Omata M, et al. Hepatol Int. 2015 Oct;9(4):486-507. doi: 10.1007/s12072-015-9630-4.

Response: We would like to thank Reviewer #1 to bring to our attention this reference. We have now cited it in our manuscript (Discussion section, page 34).

Reviewer #2:

The development of the treatment for chronic hepatitis C based on the progress of molecular biology has been remarkable, and it becomes an era when most patients are able to be cured. However, patients who can enjoy the fruits of such scientific advancement are almost restricted to developed countries. The cost of medicine is so high that the economic burden is very heavy for developing countries. For public health and medical officials, balance between eliminating HCV and economic burden is an important issue. This paper is packed with wisdom of public health and medical policy in developing countries, and this paper has never been found in top journals and is very unique.

Response: We would like to thank Reviewer #2 for the thoughtful comments and positive feedback.

Reviewer #3:

Comments for ESPS Manuscript NO 36844 This systematic review is an epidemiologic study which was designed to reveal the current status of HCV infection in the countries of the Middle East and North Africa. I think that it is a regional issue and the HCV management status differs widely among different countries. Therefore, it has less significance in clinic. In addition, language polishing is needed.

Response: We would like to thank Reviewer #3 for the comments. The new direct-acting antiviral drug (DAA) regimens cure hepatitis C chronic infection. The combination of Sofosbuvir with another DAA and the duration of the treatment depend on the hepatitis C genotype. Our overview comprehensively characterizes hepatitis C epidemiology in the 20 countries of the MENA region and emphasizes their needs in terms of treatment and prevention. This will help policy makers of these countries to develop and prioritize evidence-based strategies for prevention programs and treatment scale-up. From a global health perspective since the MENA region includes Egypt and Pakistan – the two countries with one of the highest hepatitis C burden worldwide, we believe that this manuscript will be of interest to readers of the World Journal of Gastroenterology.

The manuscript has been reviewed by the journal's preferred language editing company.