Author's response to reviews

Title: Viral Transmission Risk Factors in an Egyptian Population with High Hepatitis C Prevalence

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Author's response to reviews: see over
Response of the Authors

Reviewer’s report
Title: Viral Transmission Risk Factors in an Egyptian Population with High Hepatitis C Prevalence
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We thank the reviewers for their comments and suggestions. Changes in the revised manuscript are described below. We note that line numbers have shifted from the original version as a result of additions and deletions of text.

Reviewer: Julia Uhanova
Reviewer’s report:
The authors successfully addressed most of the issues raised with the previous reviewers. However, the paper is at times repetitive and somewhat unclear. I believe that there are a few revisions the authors can undertake to make this a stronger paper.

Major Compulsory Revisions

ABSTRACT:
Methods: The statistical analysis (line 50-51) mentions only demographic and HCV seropositivity data analysis. There is no mention of the main focus of the paper, which are the viral transmission risk factors.

Response: We have revised those lines as recommended (lines 47-48 in the revision).

Conclusions: The conclusion statement is confusing and, the way it stated, contradicts the study findings. Reading it, one may assume that the older adults contribute to the both the ongoing endemic and to the shift from a rural to urban area.

Response: We appreciate that comment and have revised the conclusion (lines 56-57) to clarify this issue.

THE MANUSCRIPT:

Introduction: The end of this section should just state the aim of the study.

Response: We have revised those lines (86-88) as recommended.

Reference to the source of the study population (lines 87-90) belongs to the Methods section and, when repeated again in the next paragraph (lines 95-97) makes the paper verbose and unfocused.

Response: We removed all mention of the source from this part of the paper.

Study Population and Data Collection: In the last statement (lines 123-125) the assessment of the current study population with the "target demographic subgroup of the Egyptian population" is mentioned. Please provide an explanation of what exactly is this target subgroup?

Response: We have removed that sentence.
Throughout the paper there are repeated references to "older" and "younger" age groups and populations. Study aim and Conclusion statement also refer to "older" population. Please define what constitutes "older age groups" in your study, as the criteria may differ for different readers. Provide this definition in the Study Population section.

**Response:** We agree with this comment, and have modified the entire manuscript accordingly. We now refer the “group born prior to 1960” rather than “older group,” and similarly avoided designating “younger” groups.

**RESULTS:**
Demographic Characteristics: this section and the corresponding tables should be rearranged. The section starts with the study results (logistic regression), followed by the description of the study demographics, and ending with more logistic regression results. Similarly, Table 1 shows the study results, followed by Table 2 with the sample demographics, and Table 3 again with the results. The sample demographics should be described first, followed by the results.

**Response:** We have changed the order of the tables and their accompanying text as recommended.

The lengthy description of migration patterns should be shortened as it adds little to the paper and makes it too wordy. The significance of the relationship between migration and HCV status is hard to evaluate without knowing the HCV status of those who did not migrate, the latter was not provided in the text or figures. Figure 1 could be supplemented by the HCV status of those who did not migrate.

**Response:** We have eliminated figure 2, but we have included migration patterns in the regression analysis as recommended by the reviewer. Please see the response to the next comment.

The logistic regression models (Table 1) include birthplace and residence at the time of interview, but even more important would be to include in the model migration vs. not. The more precise model with no migration as the reference category and different types of migration as the categories of interest with the corresponding ORs and CIs would strengthen the paper and support the focus on migration as one of the possible issues in the shifting epidemic.

**Response:** We have revised the model as recommended and added the six possible migration patterns to both the table and text (lines 174-177).

Representativeness of the Study Population: this section is better fitted within the discussion segment of the paper, as it deals with the generalizability of the study results and not directly related to the study aim.

**Response:** We have moved this section to the Discussion.

The paragraph opening (line 237-238 of the Discussion) states that "...our sample population was representative of older age groups in Egypt.." and the mentioned above assessment of HCC/EDHS populations should be moved here.

**Response:** We have done so (starting at line 204).

Limitations: Please provide reference to "many other" studies you refer to in your statement about lack of association between HCV status and transmission risk factors.
Response: We have added references to that statement (line 244).

Conclusion: the conclusion statement is not well supported by the study results. The authors clearly showed that PAT alone can not explain the high HCV prevalence. However, the results of the study did not find medical procedures to be significantly associated with the increased rates of HCV. Similarly, there is no data from this study directly supporting "informal health care settings" as possible risk factors, because there were no specific information in the questionnaire about these. Although plausible and probable, this is not a conclusion of this study, it is more of a future direction of the inquiry. Please revise this section accordingly.

Response: We have revised the Conclusion to address this concern (lines 248-254).

Minor Essential Revisions
Line 57: Remove the word "older" before "HCV positive".
Line 62: Hepatocellular carcinoma should not be a key word since this paper is about HCV and not HCC.
Line 116: add "for HCC" after "... potential environmental risk factors", because your the next sentence refers to risk factors for HCV.
Line 117: Insert period instead of comma after [10].
Table 3. Highlight unadjusted OR in blood donation category, as this is a statistically significant result: 0.76 (0.59, 0.98).

Response: We have implemented all of these minor essential revisions.

Reviewer: Abdelouaheb Bennani
Reviewer’s report:
HCV epidemiology is important, especially in Egypt. The PAT was the leading cause of this viral infection from 1950 through 1980s. What else after until recently? This paper seems to be important for this answer.

There are some relevant mistakes:
57 Conclusions: In Egypt, PAT and other transmission factors, through older (previous?) HCV positive older...

66 Chronic hepatitis C virus (HCV), a blood-borne pathogen, is a major cause of hepatocellular: “chronic” must be taken of.

72 In Egypt, the prevalence of the two major biomarkers of HCV - the HCV antibody (anti-HCV antibodies) and HCV RNA seropositivity - is estimated at 14.7% and 9.8%, respectively, in the… 75 25% for HCV RNA) [5]. The source of this epidemic has largely been attributed to the parenteral...

78 Iatrogenic sources have been considered as key contributors, especially among the elderly who...

112 collected ten milliliters of blood from participants for serological testing of HCV antibodies and HCV RNA, as well as hepatitis B virus (HBV) core antibodies and HBV surface antigen, as

Response: We have implemented all of these minor essential revisions.

128 reverse transcription (RT)-PCR to test for HCV RNA [11]. Where there were discordant results between the ELISA and RT-PCR tests, conventional PCR was used to retest for HCV RNA [10].
130 HCV positivity in this study was defined as anti-HCV and/or HCV RNA positive. This section is totally confusing! And it should be revised because it is the origin of your results! You may also describe the tests used ELISA tests are used for screening and RT-PCR is used to confirm the presence or absence of viral infection, so this viremia will discriminate between chronically infected (70-80%) and resolved infection (20-30%). You didn’t mention the reagents used for those tests.

**Response:** We have revised the paragraph on HCV testing to clarify what was done and to provide more detail (lines 124-129).

142 Among the 1764 participants, the seroprevalence of anti-HCV and HCV RNA was 29.8% and Use only prevalence because HCV RNA is not sero but molecular...

210 purposes; testing for HCV was assessed only among 15 to 59 years old individuals. Because the

**Response:** We have implemented these minor essential revisions.

Personally, I didn’t find the exact answer to risk factors other than PAT in this paper the formation of a large reservoir of infection among the adult population, which explains the high prevalence of HCV and therefore the high risk of transmission. May be if there were also young patients in the study from new born from HCV positive mothers, we would have better understand the dynamic of HCV epidemiology. Blood Transfusion was the main cause of HCV transmission before the introduction of anti HCV serology screening. Unsafe injection practices use is the leading cause both in IDUs and in low education and economic level countries.

**Response:** We appreciate and agree with these comments, and have modified the paper accordingly, particularly in the conclusions statements of the abstract and main body.