

Response to reviewers; comments

Title: Hepatitis B virus detected in paper currencies in a densely populated city of India: a plausible source of horizontal HBV transmission?

Authors: *Palashpriya Das, Ruchi Supekar, Ritika Chatterjee, Subrata Roy, Anisa Ghosh & Subhajit Biswas.*

Principal Investigator & Corresponding Author: Dr Subhajit Biswas.

Reviewer #1:

Scientific Quality: Grade E (Do not publish)

Language Quality: Grade B (Minor language polishing)

Conclusion: Rejection

Specific Comments to Authors: Applying saliva on fingers for enumerating bank notes is a common practice in the Indian subcontinent. The aim of the study is to investigate if paper currency can be the plausible mode of horizontal transmission of hepatitis B virus infection. The author found that paper notes may be a potential source of “horizontal” transmission of this virus, especially if there are cuts/bruises on the oral mucous membrane or skin but it was practically not possible to experimentally demonstrate such transmission. Detection of potentially intact/viable and “occult” HBV from currency poses potential risk of silent transmission of this virus among the general population. However, this study lack of innovation and science, and not suitable for published in this Journal.

Response: We would like to thank the reviewer for observing and explaining the salient features of our study. In response to the reviewer’s opinion that our study lacks innovation and science, we would like to point out that this is the *first report* that heavily circulating low denomination currency notes in developing and populated countries like India could be a potential means of HBV transmission, especially in places where people have the habit of using saliva for enumerating paper notes.

We also believe that the findings of this work provide one important clue to increasing incidences of HBV infection in eastern India as reported by us and others. People here are possibly getting infected with HBsAg-negative HBV strains like the ones we have described which can “silently” transmit to others in a setting where blood testing for HBV is done primarily by ELISA and NAT is not a routine practice, even before blood transfusion.

We could also demonstrate, for the first time to the best of our knowledge, large number of intact/potentially viable HBV particles present on the contaminated bank notes, by

means of immune-precipitation and Atomic Force Microscopy. We have also provided HBV-specific genetic signatures and identified the HBV mutations as OBI-specific.

Another novel scientific finding is that the HBV strains contaminating the paper currencies were found to be of HBV genotype D2 only, which appears to get fixed in the people of Kolkata “silently”. This is further supported by our previous publication “De *et al.* (2017). Occult hepatitis B virus infections (often with human herpesvirus 7 co-infection) detected in Pityriasis rosea patients: A pilot study. *Indian Journal of Dermatology*, 62, 598-605”.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: The authors of this manuscript on an excellent research topic have done a great job. These results may be highly relevant to COVID-19 infection. The recent significant rise in HBV infections in eastern India prompted the search for this virus in low denomination paper notes in a highly populated Indian city. Applying saliva on finger tips for enumerating currency notes is not only a common practice in the Indian subcontinent but common in many countries worldwide. Thus, this study is highly relevant. The authors discovered that, indeed, intact HBV particles are present in about 7.14% of the currencies and may enter either through the saliva or by microscopic skin defects. They have visual and DNA copy number confirmation of their hypothesis as well as several molecular biology tools. A small paragraph in the discussion on COVID-19 is crucial.

Response: We are thankful to the reviewer for his supportive comments and for approving our work for publication. We fully agree with the reviewer that our findings may be highly relevant towards understanding the different possible means of rapid transmission of SARS CoV-2 in densely populated cities. As per the suggestion of the reviewer, we have added a paragraph in the discussion on COVID-19 in context to our findings on HBV transmission.

Reviewer #3:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This paper report Hepatitis B virus detected in paper currencies in a densely populated city of India: a plausible source of horizontal HBV transmission. it would help to clarify a possible way for HBV transmission.

Response: We are very pleased to note that the reviewer has considered our work helpful towards clarifying a possible way of horizontal HBV transmission and has approved our work for publication.