

Responses to Reviewers' Comments.

Name of journal: *World Journal of Hepatology*

ESPS Manuscript NO: 19211

(1) The sentence “while genotype 5 has only been known to infect birds[1]”, avian HEV has ever been proposed to be listed as genotype 5, however, there is a new opinion dealing with the classification of HEV. (Smith DB, et al., J Gen Virol, 2014, 95(Pt 10):2223-32.)

Response: Thank you for the comment. We have briefly reviewed the new classification in the revised manuscript. This can be found on Page 5-6.

(2) The sentence “Genotype 4 has been reported to cause sporadic cases of acute hepatitis E in humans, which so far have been restricted to Asia (China, Taiwan, Japan and Vietnam[2, 3])” , actually, some genotype 4 HEV caused sporadic hepatitis were diagnosed in France and other European countries. (Bouamra Y, et al., Intervirology, 2014, 57(1):43-8.)

Response: Thank you for the comment. We have made a mention of the above important information in the revised manuscript. Page 6.

(3) The sentence “Chronic hepatitis E has been reported only with genotype 3 [26]” , Geng Y, et al., has just published a report on a chronic hepatitis E case caused by genotype 4 HEV. (Hepat Mon, 2014, 14(1):e15618)

Response: Thank you for the information provided. We have made a mention of the case report in the revised manuscript. Page 9.

(4) To my point of view, the title of manuscript may not be a suitable one. According to the definition of manuscript, HEV is capable of inducing CHE. Then, is CHE a kind of chronic liver diseases? This manuscript, as described by its title, is supposed to discuss the relationship between HEV infection and chronic liver disease. However, some sections, including ‘PREVENTION METHODS’, and ‘VACCINATION FOR HEPATITIS E’, seem to focus on different topics.

Response: Thank you for the comment. We have changed the title to “Chronic Hepatitis E: A Brief Review”. We agree with the reviewer that vaccination and prevention of hepatitis E may not directly pertain to chronic hepatitis E. We have put them for the

sake of completion and to educate the audience about their current status as pertaining to Hepatitis E.

(5) Except for HEV, other kinds of virus (ie. HBV, HCV) usually serve as the etiology of chronic hepatitis. Thus there is great concern about the interaction of different types of liver virus, and also chronic hepatitis related to them. Appropriate discussion about it will be appreciated.

Response: Thank you for the comment. There can be co-existence of hepatitis C and hepatitis E infection in a patient with chronic liver disease. Acute hepatitis E infection has been shown to cause flare up of liver disease in patients with chronic HCV. Similarly acute hepatitis E infection in a well compensated cirrhotic can lead to decompensated liver disease or liver failure. This has been added in the manuscript with reference. Page 11-12.

(6) Is there spoken English rather than written English in the text, such as 'If that does not work' (page 16).

Response: Thank you for the comment. This has been corrected in the manuscript.

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(7). There is no section describing the methods used for locating, selecting, extracting and synthesizing data.

Response: Thank you for your comments. We had not described the methods as our article was not written as a systematic review but rather written as a review for the clinician.

(8) There are several recent articles on chronic hepatitis E which is better to add to the manuscript to update and further strengthen the article such as: Galante et al. Relevance of chronic hepatitis E in liver transplant recipients: a real-life setting. *Transpl Infect Dis*. 2015 Jun 12. doi: 10.1111/tid.12411. [Epub ahead of print] Ramezani et al. Significance of hepatitis E virus infection in HIV-infected patients: a challenging issue. *Asian Pac J Trop Dis* 2015; 5(5): 337-341 Scotto et al. Hepatitis E virus co-infection in HIV-infected patients in Foggia and Naples in southern Italy. *Infect Dis (Lond)*. 2015 May 21:1-7. [Epub ahead of print] Ramezani et al. Hepatitis E virus infection in patients infected with human immunodeficiency virus in an endemic area in Iran. *Int J STD AIDS*. 2013; 24(10):769-74

Response: Thank you for the comments. Majority of the above papers have addressed the issue of HEV and HIV which is not the objective of our article.