

September 4, 2019

**Dear Ze-Mao Gong,  
Science Editor, Editorial Office**

Please find enclosed the edited manuscript in Word format (49818\_review.doc).

**Title: HCV clearance and less liver damage in patients with high cholesterol, LDL-c and ApoE e4 allele**

**Author:** Karina Gonzalez-Aldaco, Sonia Roman, Rafael Torres-Valadez, Claudia Ojeda-Granados, Luis Alberto Torres-Reyes and Arturo Panduro.

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

**ESPS Manuscript NO:** 49818

In general, the manuscript was revised completely. Each point by point comment was modified or corrected according to the reviewers' petitions. Revision was done according to the suggestions of the reviewers and highlighted in the text where appropriate.

**Reviewer #1 (02567669):** This retrospective study describes parameters of lipid metabolism as factors that predispose to spontaneous clearance of HCV infection: LDLc and APOEepsilon4. The association is particularly striking in overweight persons. The study is well designed and performed. The conclusions seem to be sound. The authors try to explain the observed effects by the known mechanisms of entry of the virus into hepatocytes. Due to the complexity of this process it is difficult to ascribe the present data to one or more of the different steps of viral lifecycle. However, the data of this manuscript deserve to be published. Few spelling errors must be corrected.

1. English language was revised and corrected. The co-author Sonia Roman is a native speaker of the English language.

**Reviewer #2 (03253490):** Gonzalez-Aldaco K et al. aimed to investigate the role of APOE -ε2, -ε3, and -ε4 alleles and the metabolic profile in the outcome of HCV infection in this retrospective study. The study is interesting. The manuscript is well written. I think it has enough priority for publication. Thank you for having allowed me to review this manuscript.

1. Thank you for your comments. English language was revised.

**Reviewer #3 (01805500):**

**1. On the basis of some laboratory and anthropometric data, is it possible that some patients suffered from NAFLD. Are available data on this aspect, i.e., US?**

**A1)** Yes, some patients had NAFLD, but there were no differences between groups. Regarding this point, we published the prevalence of NAFLD/NASH in young and obese adults (Sepulveda-Villegas M et al; PLoS One. 2019 Jan 4;14(1):e0208926.). Since NASH is associated to genetic factors, further studies are necessary to analysis if patients with HCV have genetic predisposition for NASH.

**2. At the light of HCC incidence also in HCV carriers the main role of metabolic syndrome is a factor to not be overlooked as per....Could metabolic syndrome lead to hepatocarcinoma via non-alcoholic fatty liver disease? World J Gastroenterol. 2014 Jul 28;20(28):9217-28.**

**A2)** Yes, we agree with the reviewer, that metabolic syndrome is a risk factor that can lead to HCC. Interestingly, overall HCC incidence in Mexico is very low, given the fact that most cirrhotic patients die prematurely before latent HCC is detected (Roman et al, Journal of Cancer Therapy, 2013, 4, 367-376). Therefore, this point was not discussed.

**3. Some data show a large SD and should be controlled for their distribution (S-W test).**

**A3)** The normal distribution of the quantitative variables with a number greater than 30 cases was tested with Kolmogorov-Smirnov test. While, the normal distribution of the quantitative variables with a number of cases less than 30 was tested with the Shapiro-Wilks test. All variables followed normal distribution and therefore were analyzed using parametric statistics. This explanation was added: The use of the Shapiro-Wilks test was described in the statistics section, page 9.

We greatly appreciate the editorial work of the reviewers to enhance our work.

Best regards,

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