

Format for ANSWERING REVIEWERS



January 18th, 2016

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 23901-review.doc).

Title: Hepatogenous Diabetes. Is it a neglected condition in chronic liver disease?

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Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 23901

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated.

Language editing modifications appear marked in blue .

Manuscript modifications according to reviewers' comment appear marked in yellow

Added references appear marked in yellow on the manuscript.

2 Revision has been made according to the suggestions of the reviewers:

1.- **Reviewer's code:** 00053485

A.- The reasons why we think that hepatogenous diabetes is a neglected condition are clearly discussed in the manuscript and we think they are easy to understand. Therefore, **we did not consider necessary to make a Table exposing them.**

B.- According to reviewer's comment we added a discussion regarding diabetes mellitus with hepatocellular carcinoma association as well as prognosis of patients. We included the following references recommended by the reviewer:

-**Sumie S et al** Significance of glucose intolerance and SHIP2 expression in hepatocellular carcinoma patients with HCV infection. *Oncol Rep* 2007;18:545-552

-**S. Schlesinger,** et al Diabetes mellitus, insulin treatment, diabetes duration, and risk of biliary tract cancer and hepatocellular carcinoma in a European cohort. *Ann Oncol* 2013;24:2449-2455.

C.- Etiological discussion in insulin resistance/diabetes mellitus with HCV was stated and described according reviewer's comments. We added the suggested references made

by the reviewer:

-Kawaguchi T et al. Hepatitis C Virus Down-Regulates Insulin Receptor Substrates 1 and 2 through Up-Regulation of Suppressor of Cytokine Signaling 3. *Am J Pathol* 2004;165:1499-1508

-Parvaiz F et al. Hepatitis C virus NS5A promotes insulin resistance through IRS-1 serine phosphorylation and increased gluconeogenesis. *World J Gastroenterol* 2015;21:12361-12369.

-Kawaguchi T et al. Clearance of HCV Improves Insulin Resistance, Beta-Cell Function, and Hepatic Expression of Insulin Receptor Substrate 1 and 2. *Am J Gastroenterol* 2007;102:570-576.

D.- We included a discussion regarding the association of exogenous insulin or sulphonylurea treatment with an increased incidence of hepatocellular cancer on the manuscript as suggested by the reviewer. In this topic, we added the following reference also recommended by the reviewer:

-Singh S, Singh PP, Singh AG, Murad MH, Sanchez W. Anti-diabetic medications and the risk of hepatocellular cancer: a systematic review and meta-analysis. *Am J Gastroenterol.* 2013; 108: 881-891.

2.- Reviewer's code: 00068156

Thanks to reviewer comments. The reviewer suggested no modifications.

3.- Reviewer's code: 00069340

A.- Clinical manifestation and biochemical parameters of HD were added to the manuscript as it was recommended by this reviewer.

For support of these concepts we added the following reference:

-Kim MG, Choi WC. [Differential diagnosis of diabetes mellitus caused by liver cirrhosis and other type 2 diabetes mellitus] *Korean J Hepatol* 2006; **12**: 524-529

4.- Reviewer's code: 00005258

A.- We are convinced that this manuscript is strongly compatible with an editorial since it is a critical analysis of published manuscripts regarding HD. At the same time, we give on the text our point of view regarding the present and the future of this clinical condition.

B.- English language was revised

5.- Reviewer's code: 00185907

A.-Orthographic mistakes of the manuscript underlined by the reviewer were corrected.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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