

Porto Alegre, December 25, 2017.

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Dear Editor of WJG,

We thank you very much for the comments from the reviewers. They have indeed shown great knowledge in this field and have remarkably contributed for the improvement of this manuscript to be published in such well-recognized journal. All of the comments are of great importance and interest to us, and we tried to address them by answering all questions.

We also carry out the revision of the language again with our translator, according to the attached statement.

All the answers are itemized below by the reviewer code.

Best Regards,

The Authors

## **Answers:**

**Reviewer code: 03262379**

- 1. I suggest to exclude the data for survival of patients from the last part of results and also the part from discussion given it is unrelated to the main aim of the study.***

Thank you for the contribution. We excluded the survival data from the Results and the Discussion and suppressed the figure that represented this data (Figure 2)

- 2. Can authors present how treatment of HBV or HCV and also sustained response to treatments impacted the HCC development in this study?***

Unfortunately, although we recognize the importance of these variables, it was not possible to show their impact due to the small number of cases with information in the medical records, mainly in relation to HBV. Note also that the small number of cases with HCC (36) would impair an adequate analysis. Thus, the attempt to place the treatment and sustained virological response (SVR) in a statistical model was not feasible. However, general treatment data are presented in Table 1 and the description of general SVR is cited in the Results (SVR HBV coinfecting 54.8% vs 92.3% in mono-infected patients,  $p = 0.012$ ; SVR HCV coinfecting 44.3% vs 56.2% in mono-infected,  $p = 0.083$ ).

- 3. It is important to emphasize that this study was conducted on patients referred to tertiary care center.***

This data is already included in the Study Design. To emphasize this, we add an observation in the first sentence of the Results.

- 4. Patients with hepatitis B routinely stratified based on clinical and laboratory findings in groups of patients with active, inactive and etc needing a range of managements such as antiviral therapies. It is why I guess just a proportion of patient without HIV underwent antiviral therapy while patients with HIV should be treated with common antiviral therapies of both infection and so most of them were actively treated. I suggest authors to present the clinical presentation of patients with hepatitis B in both group if the data available.***

In contrast to other parts of the world, HBV infection does not play a prominent role in our country - a prevalence of less than 1% according to Ximenes et al (Am J Trop Med Hyg 2015; 93 (6): 1341-1348). In the present study, we also found a few number of HBV patients (82 HIV/HBV and 49 HBV - Table 1). Seventy-seven HBV/HIV coinfecting patients received antiviral therapy (we agree that many being part of the HIV therapy) and 13 HBV monoinfected patients received specific therapy because presented active disease in clinical and laboratory evaluation. Unfortunately, it was not possible to make considerations about treatment due to the small number of cases evaluated, as already described in the Results.

**Reviewer code: 00503560**

- 1. As is well known, the incidence of HCC is different among patients infected with HBV and HCV. Therefore, the authors should compare the incidence between HIV/HCV coinfecting patients vs. HCV monoinfected patients, and HIV/HBV coinfecting patients vs. HBV monoinfected patients. In this cohort, the number of HBV infected patients is low. The authors should show the results of subanalyses only in HCV infected patients with or without HIV infection. If impossible, the authors should describe regarding that as a limitation.*

Hepatitis B is a low endemicity disease in our region. Ximenes et al in 2015 (Am J Trop Med Hyg 2015; 93 (6): 1341-1348) found a prevalence about <1%. The present study corroborated this data: 804 patients were included and only 131 were HBV positive (82 HIV coinfecting). When we analyzed the 36 HCC cases, only three patient had HBV (1 HIV/HBV coinfecting and 2 HBV monoinfected). In this context, we attempted to analyze the incidence of HCC considering only HIV/HCV coinfecting vs HCV monoinfected and there were no differences regarding the already described findings in Results. We added this information in Results and an observation as a limitation in relation to these aspects of the study at the end of the Discussion.

- 2. As is well known, the elimination of HCV and the suppression of HBV can reduce the incidence of HCC. Therefore, the authors should consider this and carry out the present analyses. The authors should mention this in the discussion.*

Unfortunately, although we recognize the importance of these variables, it is not possible to present this data due to the small number of cases, mainly in relation to HBV. Note also that the small number of cases with HCC (36) would impair an adequate analysis. Thus, the attempt to place the treatment and sustained virological response (SVR) in a statistical model was not feasible. However, general treatment data are presented in Table 1 and the description of general SVR is cited in the Results (SVR HBV coinfecting 54.8% vs 92.3% in monoinfected patients,  $p = 0.012$ ; SVR HCV coinfecting 44.3% vs 56.2% in monoinfected,  $p = 0.083$ ). This limitation was now observed at the end of the Discussion

**3. In the note of Table 4, the authors should correct "CHC=Hepatocellular carcinoma" to "HCC=Hepatocellular carcinoma".**

I'm sorry for the mistake. It has been corrected.