Author's response to reviews

Title: Infection by the hepatitis C virus in chronic renal failure patients undergoing hemodialysis in Mato Grosso State, Central Brazil: a cohort study.

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Author's response to reviews: see over
Dear Editors
BMC Editorial team,
we have reviewed the manuscript 4674206381091069 and submitted it to an English-speaker editor. This letter brings the answer to the referees questions.

1st Referee

Major Compulsory Revisions
1.- Importance for the author the isolation measures. 1.a.- staff only for HCV patients or not?
A: Both referees have asked for more information about the hemodialysis conditions and routine. Previously we had not provided information about control measures issues because we had worried about space in the periodic and because our data about that was not individualized. Now, we have introduced throughout the text (results and discussion) information about biosafety on studied hemodialysis units obtained from nurses responsible for the staff. The specific answer for this Ms. Barril question is that there were some difference between units.

2.- Importance of RPC in relation viral load (HCV-RNA presence)
A: Molecular biology tests were not routinely provided to screening these patients in our region. Since we were interested in HCV exposure more than HCV viremia (epidemiological approach), we had decided to work with anti-HCV EIA results. We introduced commentaries in methods and discussion about advantages and disadvantages of deal with serology or molecular biology. We have included the following commentary in Discussion:

“Polimerase chain reaction is considered the gold standard test to confirm HCV viremia. However, this method is still expensive to be performed as a screening test in most of developing countries. In Brazil, immunoenzymatic assays (EIA) are routinely employed in blood banks and hemodialysis units to search for HCV-infected patients. Although anti-HCV positivity by EIA does not discriminate between patients with HCV viremia and those who had HCV cleared, it is very sensitive and may occasionally identify hemodialysis patients with very low viremia not detected by PCR. Aiming to increase EIA specificity only successively positive anti-HCV patients were considered as a case in the present study. Furthermore, the positive predict value of anti-HCV by EIA increases in high prevalence settings such as hemodialysis environment. Some of the anti-HCV positive patients detected in the first evaluation could have already had the HCV cleared. Since our goal was assessing prevalence of infection instead of viremia, EIA was more appropriate than PCR.”

3.- Consider the risk factors in some unit independent number HCV+ patients to increased number seroconversion, isolation measures in these centers.
A: We have informed above that our results about control measures issues were collected by hemodialysis units more than by patients. The three units that failed to regularly apply biosafety recommendations presented the highest prevalence and incidence rates of anti-HCV. This information was supplied through the revised text.

4.- Evolution of the incidence in different group.
A: We are sorry because we did not understand the exact meaning of this topic, since we provided Kaplan Meier curves of the entire group and the two groups of units. Maybe the referee has asked for a new graphic with individualized curves of each unit, but it did not add new aspects to the text and we would rather did not include another graphic to the
article. Maybe the referee has asked for other kind of categorization. In this case, please let us know specifically which variables should be presented.

5.- Improve bibliography and correlation with inclusion in the redaction.
A: We have introduced more references and have tried to improve its correlation with the text.

2nd Referee

Major Compulsory Revisions
- Findings of this study are interesting but not original. There is no insight on the causes of HCV-Ab seroconversion, including intra- and extra-dialysis factors.
- Indeed, the Authors gave no information on the infection control measures and practices in those units that had a higher prevalence rate. What about understaffing?
A: We have amended the text in order to improve the discussion about intra- and extra-dialysis factors influencing HCV transmission. We have added a new Table (2) with information of control measures by unit, including if the unit provided dedicated staff to HCV infected-patients or not. We have introduced commentaries in the text like that: “All analysed units adopted the use of dedicated machines to isolation of anti-HCV patients. In spite of that, three units presented higher prevalence and incidence of HCV infection. These findings reinforce the need for the adoption of further control measures, as shown elsewhere [8,20,22]. Our research points out that these three units failed to apply other recommendations, such as do not share items and staff, and discard gloves and wash hands between each patient and station...”

We did not report data about some risk factors in the first version of the text because there is no association in univariate analysis. Commentaries about extra-factors such illicit drug use and previous surgery procedures were provided in Discussion: “Risk factor classically associated with HCV transmission such as illicit drug abuse and promiscuous sexual behaviour were seldom reported by participants and did not show association with anti-HCV positivity. Petrosillo et al (2001) have reported an increased risk of HCV infection in hemodialysis patients submitted to surgery procedures in the previous six months in an Italian multicenter study [27]. In the present study, this variable was also rarely reported, precluding statistical analysis...”

Conclusions are too general and misleading. What is the role of the environment in HCV infection? Maybe the main cause is a break in infection control measures but we have no information on the differences in the two groups of dialysis units. Moreover, there is no information on the use of shared equipment of items. Indeed, it seems as in some units with a high HCV prevalence and incidence rates there is an epidemic factor not investigated by the authors.
A: We tried to improve the final text of discussion including commentaries on data obtained from nurse staff. We think the main factors possibly implicated in HCV transmission in hemodialysis environment, such as control measures, length of hemodialysis therapy, and HVC infected-patients rates of each unit have been approached in the present version. In fact, it is possible that there is another non-investigated factor influencing the HCV rates by unit. However, we think that the introduction of data and
commentary about failed in adoption of infection control measures may justify the infection distribution.
- The Authors wrote that isolation of HCV-Ab positive patients was applied both in the units with higher and lower incidence rates. This is a confirmation that environment had no role in HCV spread in the units.
A: Dedicated machines is on the several measures recommended to avoid HCV circulation in hemodialysis environment. We think the added data about lack of adoption of control measures support the statement that most of the new HCV infections were acquired in the studied units with higher HCV prevalence.
- Finally, there is no information on extradialysis factors such as surgical procedures, as evidenced in other studies.
A: This information was provided.
Minor Essential Revisions
- The background in the abstract is not a background
A: We are very sorry about our confused abstract’s background. A new one was provided.
- English should be edited.
A: The new text was submitted to a English-speaker editor.

We are looking forward to the BMC decision and we are ready to review the manuscript again if the referees consider it necessary.