Response to reviewers

First of all, I express my deep thanks to the reviewers who they well assessed the manuscript. The notes which were raised during the reviewing process enrich the article concerning the scientific and language issues. I took all the raising comments into consideration in the revised manuscript. I highlighted the required changes in a yellow color. I hope the changes made in the revised form are satisfactory for the reviewers and the study will be accepted for publication in the esteemed journal "World Journal of Meta-Analysis".

Best regards

Professor Dr. Raid M. Al-Ani

Reviewer #1:

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: The authors summarized the various aspects of hepatic involvement during the COVID-19 course or following its vaccination in this mini-review.

Ok, thank you.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Major revision

1 the topic is Liver dysfunction-related COVID-19: A narrative review the authors should focus the liver injury caused by COVID-19 rather than the other factors, it is true that many factors such as drugs can cause liver dysfunction, in this paper, the topic is SARS-CoV-2 induced liver dysfunction. it is highly to expect the authors to focus this point, SARS-CoV-2 caused liver injury, explain riefly the difference from liver injury caused other disorders. please consider to reduce or delete the unrelated section such drug induced liver-injury.

Thank you for your outstanding comment. I made the required changes by reducing around 5 pages from the text.

2 the conclusion includes "Hepatic involvements determine the severity of COVID-19. Abnormal liver function tests are more in non-survivors than survivors." please show the specific data or evidence in the text.

This sentence "a significant relationship has been illustrated between SARS-CoV-2-related mortality and preexisting severe liver cirrhosis resulting in a rise in the mortality percentage[107]." is the evidence in the text to support what was written in the conclusion.

3 please explain what is NAFLD?(Another liver disease NAFLD also exists in COVID-19 patients and has more potential for liver dysfunction. The increased risk of NAFLD with severe COVID-19 has presently more than in non-NAFLD patients)

Thank you for your nice comment. I explained this issue as in the following:

The metabolic syndrome nonalcoholic fatty liver disease (NAFLD) which is the most frequent CLD has a highly raised risk for severe COVID-19, it was estimated in a meta-analysis of epidemiological studies with 5.2 fold increased risk of severe COVID-19 [55]. A recent study by Jiling and his colegues has reported that the significant accociation was recorded between NAFLD and severe COVID-19 with the risk factors (male sex an old age) as well the casual risk factor obesity, while the other metabolic pertubations (diabetes melitus and hypertention) does not have accociation with severe COVID-19[56]. CRP, D-dimer, and ferritin levels as wel as lymphocyte and neutrophil count are smillar for both NAFLD and non-NAFLD patients. The liver parameters such as serum albumin, ALP, serum bilirubin levels are comparable across both groups. In contrast, the increased consentrations of ALT, AST and GGT have observed in NAFLD patients compared to non-NAFLD patients. The mortality and hospitalization stay have not increased in COVID-19 patients with NAFLD based on increased liver parameters [57].

A study by Pan et al. has illustrated liver injury for COVID-19 patients with NAFLD; it has found that liver injury happened in 50% and 75% of infected persons upon admission and during staying in hospital, respectively. These findings are due to the increased expression of ACE-2 receptor as well as chronic inflammation of the liver in NAFLD, which leads to liver injury[58]. In addition, the degree of liver fibrosis in NAFLD may affect the consequence of SARS-CoV-2; such the high or intermediate scores of FIB4 has associated with severe SARS-CoV-2 illness among patients with MAFLD[59].

4 pelase expalin the relationship of lung injury and liver injury caused by COVID-19.

I explained this subject as below.

The over-activation of the immune system, which is correlated with COVID-19, might be included in liver injury. A significant increase in serum inflammatory cytokine concentrations, including interferon-γ, IL-1β, IL-10, IL-6, tumor necrosis factor (TNF), and soluble IL-2 receptor, exist in subjects with SARS-CoV-2, particularly those patients with severe pneumonia[45,46].

5 there are many grammer errors, that is difficult to understant, such as

I am sorry for such mistakes. I solved this subject either by removing the sentences through the reduction process as you suggested or rephrasing the sentences to be more clear for example:

By the 11th of March 2020, a declaration by WHO that COVID-19 is a global pandemic

The WHO declared that COVID-19 is a pandemic on March 11, 2020.

In treating the previous underlying hepatic diseases, such antiviral drugs for treating HBV or HCV could interfere while healing COVID-19 resulting in HCV and HBV viral activity and aggravating liver inflammation[32]

In patients with coexisting COVID-19 and previous history of HBV, HCV, and liver cirrhosis, there might be a synergistic effect between the drugs used for these diseases with the drugs used for the COVID-19 treatment. As a consequence, acute hepatitis happen[48].