

Reviewer #1:

1. The manuscript is very well written - it needs a comprehensive review by an expert statistician to be published.

The review has been written by authors Author Salim Surani who has a master's degree in public health and health Management and Dr. Rahul Kashyap who is a research director and teaches biostatistics and research. The statistical analysis was done by Dr. Vikas Bansal who also has a master's degree in Public health services management. He has completed the course "Introduction to Systematic Review and Meta-Analysis" by Johns Hopkins University and published more than nine systematic reviews and Meta-analysis with many ongoing projects.

Reviewer #2:

1. Which criteria did the authors use to diagnosis NAFLD? Were the patients diagnosed with NAFLD prior to admission or after admission?

Patients were diagnosed with NAFLD based on FIB-4 scores, Fatty liver index, Hepatic steatosis index scores, Liver biopsy, Fibro scan, Hepatic-To-Splenic Attenuation Ratio, Liver stiffness Measurements and CAP With a Fibro scan, hepatic steatosis on any prior imaging, Fibrosis by Magnetic Resonance Elastography, liver attenuation index (LAI). We only included patients that were diagnosed with NAFLD prior to the index admission. Table one describes the method of diagnosis of NAFLD for each included study. We thank the author for the comment. We have included this information in our methods section.

2. Some studies only used FiB4 to measure NAFLD. Was it accurate?

FIB-4 score has close to an 86.36% sensitivity of diagnosing NAFLD and a positive predictive value of around 90%. We only included studies that measured FIB-4

prior to admission since alteration in LFTs during COVID infection could falsely elevated FIB-4 scores. We have also included a statement in the limitations of the study stating that since bio-marker, lab assessments are not gold standard for diagnosis of NAFLD. There may be misclassification of patients with and without NAFLD. We thank the reviewer for noting this and helping improve our manuscript.

3. In study 25 and 26, the number of patients with NAFLD was much more than the patients without NAFLD. Was this correct?

Yes, the numbers are correct.

4. The authors should notice that the level of medical care at each medical clinic was different, and this could lead to different levels of disease severity and death.

We thank the reviewer for this information and agree on this. We have included this in our and limitations now.

Reviewer #3:

1. The authors considered patients with MAFLD and NAFLD in the same group. However, there are important differences between these two groups. Do the authors believe that these differences could not interfere with the evaluated outcomes?

We thank the reviewer for bringing up this point. We agree that patients underlying medical conditions and co-morbidities that are component of metabolic syndrome would also interfere with the evaluated outcomes. We understand that since our meta-analysis

is based on retrospective studies, patients between studies and within studies are different which can influence the outcome differently. Further in many of the studies on NAFLD, the patients had co-morbidities of metabolic syndrome. We agree this is a limitation of our study. Studies are emerging that Non-alcoholic fatty liver disease (NAFLD) is mutually and bidirectionally linked with metabolic syndrome. Furthermore, there is an ongoing debate about renaming NAFLD to metabolic dysfunction-associated fatty liver disease, which is more appropriate and inclusive. This is because NAFLD is a heterogeneous disease with pathogenesis involving both genetic and metabolic factors. We can also describe NAFLD to be in the pathway between metabolic syndrome and MAFLD. We agree on the authors information and insight. We have included this information in our methods section and the limitations of our study now.

2. It is important to note that all patients with MAFLD (+)/NAFLD (-) had a second aetiology for liver disease. Could liver disease superimposed on fatty liver disease interfere with COVID outcomes?

We excluded studies that had patients with other underlying causes for liver diseases including alcoholic liver disease. We understand that there are limitations to retrospective studies and there may be unknown medical history/underdiagnosis or misclassification of patients in studies. We included this in our limitations now.

3. Do the authors consider that the stage of liver disease (hepatic cirrhosis) might influence COVID-associated outcomes?

We only included studies in our manuscript that compared mild or No liver disease to moderate and severe liver disease. We excluded studies that did not use this comparison so we could maintain a degree of homogeneity. We understand the methods used to diagnosed NAFLD are not gold standard and there may be some misclassification of patients on both sides.

4. Concerning the methods, I would suggest taking into account the following points: • "Garbage in, garbage out". The disadvantage of a meta-analysis is that it puts a "weak

paper" in a fancy-looking package and can mislead both you and your readers. Heterogeneity begins when considering patients with MAFLD and NAFLD in the same group. In addition, liver fibrosis severity (presence and severity of cirrhosis) should be considered. These critical issues that could affect the findings of the meta-analysis, should lead to a more cautious conclusion.

We have changed our conclusion to be more hypothesis generating and cautious. We thank the reviewer for this observation and for helping improve our manuscript.

5.The authors stated that the study search had been performed to July 2022; however, the pre-specified protocol (related to the link indicated in the material and methods section) was dated March 2022. Have the authors updated the search and consequently added new records?

Yes, we updated the search prior to starting manuscript writing and found newly added studies to literature that met our inclusion criteria. They were included in our study. We have updated the protocol in Prospero.

6.Although excluding clinical trials reported in languages other than English from meta-analyses may introduce bias (speech distortion). For the sake of clarity, this limitation should be reported for discussion.

Thank you for the insight. Agree this could lead to bias. We have now mentioned this in our limitations.

Reviewer #3:

The manuscript is very well written - it needs a comprehensive review by an expert statistician in order to be published

1. The title of the manuscript is too long and must be shortened to meet the requirement of the journal (Title: The title should be no more than 18 words).

Shortened title:

Association of Non-alcoholic fatty liver and Metabolic-associated fatty liver with COVID-19 Outcomes: A systematic review and meta-analysis.

2. Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, “Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...”.

Done

3. Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file.

Done

4. Please authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden.

Done

5. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned.

Done

6. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper).

Done

7. If the picture is ‘original’, the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT):
Copyright ©The Author(s) 2022.

Done

8. Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the Reference Citation Analysis (RCA). RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.>

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