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| Manuscript Title | Abnormal liver chemistries as a predictor of Coronavirus Disease 2019 severity and clinical outcomes in hospitalized patients in a Major U.S. Hospital Network |
| Study Type | Retrospective Cohort Study |
| Authors | Arunkumar Krishnan, Laura Prichett, Xueting Tao, Saleh A. Alqahtani, James P Hamilton, Esteban Mezey, Alexandra T. Strauss, Ahyoung Kim, James J. Potter, Po-Hung Chen, Tinsay A.Woreta |
| Journal | World Journal of Gastroenterology |
| Manuscript Number | 68287 |

SCIENTIFIC QUALITY:

Please resolve all issues in the manuscript based on the peer review report and make a point-by-point response to each of the issues raised in the peer review report. Note, authors must resolve all issues in the manuscript that are raised in the peer-review report(s) and make point-by-point responses to each of the issues raised in the peer-review report(s), which are listed below.

Answer: Thank you so much for taking your time and review our manuscript and sharing your comments. We have addressed and resolved all issues in the manuscript based on the peer reviewers' reports/comments. We have included our response in the table below and consecutive pages in this draft to answer the editorial team members' comments.

| S. No. | Reviewer / Section | Comments | Response |
|-----------------------------|--------------------|--|--|
| Peer Review Comments | | | |
| 1 | Reviewer #1: | <p>Scientific Quality: Grade C (Good)</p> <p>Language Quality: Grade B (Minor language polishing)</p> <p>Conclusion: Minor revision</p> <p>Specific Comments to Authors: well written article and interesting points.</p> <p>Just to clarify;</p> <p>1) in abstract, the use of the word other races seems includes?</p> | <p>-Thank you so much for taking your time and review our manuscript and sharing your comments. We appreciate that</p> <p>-We have made the following changes in the manuscript based on your valuable comments:</p> <p>Others are mostly based the patient who are not included in the major race category as White, Black, Asian and Other.</p> <p>So, "Other race" is including the</p> |

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| | | <p>2) methods : advise to include ct value cut of point for positivity as threshold differs between countries</p> <p>3) clinical classification of covid-19 pneumonia : under severe, resting O2 sat of less than 43% is unlikely the right level in guidelines. Please recheck that it is 93%.</p> | <p>patients who are in either one of the following categories: Hispanic, American Indian or Alaska Native, Other Native Hawaiian or Other Pacific Islander, Unknown and Two or more races</p> <p>2) Different molecular assays are used for SARS-CoV-2 detection including the NeuMoDx (Qiagen), cobas (Roche) , Aptima (Hologic), the Xpert Xpress SARS-CoV-2/Flu/RSV (Cepheid), the ePlex respiratory pathogen panel 2 (GenMark) , the Accula, and the RealStar SARS-CoV-2 assays (Altona diagnostics).</p> <p>Assays used for diagnosis have received the FDA- EUA and the laboratory follows the assays' package inserts. For reporting positives, predetermined manufacturers' cut-offs are used that differ based on the platform used.</p> <p>However, Only laboratory-confirmed patients were included in this study.</p> <p>3) Thank you for pointing out, we have corrected the fingertip oxygen saturation < 90% based on Clinical management of COVID-19; Interim guidance</p> |

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| | | <p>4) what are the confounders? please specify</p> <p>5) regression analysis should clearly state the direction, value, significance</p> <p>6) table 2, 3, 5: under liver biochemistries, p-value not accurately displayed as it was mentioned in a whole category instead of individual (eg. all level of abnormalities bundled in together)</p> | <p>4) The confounders are Age, gender, ethnicity, race, body mass index, and all the preexisting comorbidities, and they were adjusted in the Multivariable Cox proportional hazards model. We have added this text in the statistical analysis section in the main text and in legends of tables 4 and 5.</p> <p>5) We have included the statement about the regression analysis in the main text with value, significance, and directions and also stated the results in detail in Tables 4 and 5. However, we have included the importance and significance of abnormal levels(directions) of liver chemistries and mechanical ventilation in the main text, but table 4 has clear values.</p> <p>6) In table 3 and 5, under the liver biochemistries, the comparison was done between the different levels of liver injury and was categorized based on the degree of liver enzyme elevation as mild (1-2 times of ULN), moderate (>2-5 times of ULN), and severe (>5 times of ULN), since the comparison was done between this category, so we have given one p-value and instead of individual, but in table 2 p-values are mentioned based on the individual comparison between the patients with nonsevere and severe diseases</p> |

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| 2. | Reviewer #2: | <p>Scientific Quality: Grade B (Very good)</p> <p>Language Quality: Grade A (Priority publishing)</p> <p>Conclusion: Accept (General priority)</p> <p>Specific Comments to Authors: I have read the manuscript entitled Abnormal liver chemistries as a predictor of COVID-19 disease severity and clinical outcomes in hospitalized patients in a Major U.S. Hospital Network, submitted to the World Journal of Gastroenterology. In this paper, the authors aimed to assess the prevalence of elevated liver chemistries in hospitalized patients with COVID-19 and compare the serum liver chemistries to predict the severity and in-hospital mortality.</p> <p>This paper is quite well written and I have no questions to ask.</p> | Thank you so much for taking your time and review our manuscript and sharing your comments. We appreciate that |

4 LANGUAGE QUALITY

Please resolve all language issues in the manuscript based on the peer review report. Please be sure to have a native-English speaker edit the manuscript for grammar, sentence structure, word usage, spelling, capitalization, punctuation, format, and general readability so that the manuscript's language will meet our direct publishing needs.

Answer: We have done meticulous proofreading, and language is polished to meet the publishing needs

5 ABBREVIATIONS

In general, do not use non-standard abbreviations, unless they appear at least two times in the text preceding the first usage/definition. Certain commonly used abbreviations, such as DNA,

RNA, HIV, LD50, PCR, HBV, ECG, WBC, RBC, CT, ESR, CSF, IgG, ELISA, PBS, ATP, EDTA, and mAb, do not need to be defined and can be used directly. Now we list the abbreviations rules as follows.

(1) Title: Please spell out any abbreviation in the title. Abbreviations are not permitted.

Answer: We have spelled out any abbreviation in the title. Since the abbreviations are not permitted.

(2) Running title: Please shorten the running title to no more than 6 words. Abbreviations are permitted.

Answer: We have shortened the running title with 6 words

(3) Abstract: Abbreviations must be defined upon first appearance in the Abstract.

Examples: Example 1: Hepatocellular carcinoma (HCC). Example 2: Helicobacter pylori (H. pylori).

Answer: We have defined the abbreviations when they first appear in the abstract; however, the lab parameter like ALT, AST, T-Bil, and ALP not defined since they are commonly used abbreviations

(4) Key words: Abbreviations must be defined upon first appearance in the Keywords.

Answer: We have defined the abbreviations in the Keywords

(5) Core tip: Abbreviations must be defined upon first appearance in the Core tip.

Examples: Example 1: Hepatocellular carcinoma (HCC). Example 2: Helicobacter pylori (H. pylori)

Answer: We have defined the abbreviations when they first appear in the core tips; however, the lab parameter like ALT, AST, T-Bil, and ALP not defined since they are commonly used abbreviations

(6) Main Text: Abbreviations must be defined upon first appearance in the Main Text.

Examples: Example 1: Hepatocellular carcinoma (HCC). Example 2: Helicobacter pylori (H. pylori)

Answer: We have defined the abbreviations upon first appearance in the entire Main Text

(7) Article Highlights: Abbreviations must be defined upon first appearance in the Article Highlights. Examples: Example 1: Hepatocellular carcinoma (HCC).Example 2: Helicobacter pylori (H. pylori)

Answer: We have defined the abbreviations upon first appearance

(8) Figures: Please verify the abbreviations used in figures and define them (separated by semicolons) at the end of the figure legend or table; for example, BMI: Body mass index; CT: Computed tomography.

Answer: We have included the abbreviations used used in figures and define them (separated by semicolons) at the end of the figure legend.

(9) Tables: Please verify the abbreviations used in tables and define them (separated by semicolons) at the end of the figure legend or table; for example, BMI: Body mass index; CT: Computed tomography.

Answer: We have included the abbreviations used in tables and defined them (separated by semicolons) at the end of the table