Rapid Reviews COVID-19

Review 1: "Variants in SARS-CoV-2 Associated with Mild or Severe Outcome"

Min Xie¹

**¹Tongji Hospital of Tongji Medical College of Huazhong University of Science and Technology,
Department of respiratory and critical care disease, China**

Published on: Jul 05, 2021

License: [Creative Commons Attribution 4.0 International License \(CC-BY 4.0\)](https://creativecommons.org/licenses/by/4.0/)

RR:C19 Evidence Scale rating by reviewer:

- **Potentially informative.** The main claims made are not strongly justified by the methods and data, but may yield some insight. The results and conclusions of the study may resemble those from the hypothetical ideal study, but there is substantial room for doubt. Decision-makers should consider this evidence only with a thorough understanding of its weaknesses, alongside other evidence and theory. Decision-makers should not consider this actionable, unless the weaknesses are clearly understood and there is other theory and evidence to further support it.

Review:

The authors evaluated the association of SARS-COV-2 variants with the severity of COVID-19 from the database of GISAID. The topic is interesting to the readers especially considering the current epidemic involved with several new SARS-COV-2 variant strains. While there are still some major concerns:

1. Although the authors stressed the big number of 155,958 SARS-COV-2 genomes downloaded from GISAID database, only 3637 sequences were evaluated in this study according to the aims and method stated in the manuscript. The big gap draws attention to whether the results of this study could be representative of the actual prevalent variants around the world.
2. Generally, COVID-19 patients would consist of around 80% mild cases and 20% severe cases. While in this study, the population had 2870 severe cases and 767 mild cases. The reason may due to the higher probability of severe cases to be tested for virus genome. However, the imbalance of the severe/mild ratio would lead to the bias of the result, especially considering the statistical complexity.
3. When evaluating the severity of COVID-19, the criteria are extremely important and critical for the interpretation of the results. In this study, the severe cases included "deceased," "hospitalized," "ICU," and "pneumonia." It would be quite confusing. For example, COVID-19 pneumonia could be a mild disease in clinical practice. Another concern is some COVID-19 patients were hospitalized because of their underlying disease, while not for the severe COVID-19 condition. Such issues happened frequently in nursing homes or with elderly patients. Thus, the authors need to address a clear definition of severe COVID-19 and make an appropriate classification of subjects.