Review of: "Molecular detection of SARS-CoV-2 from indoor air samples in environmental monitoring needs adequate temporal coverage and infectivity assessment"

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Potential competing interests: The author declared that no potential competing interests exist.

First of all, it is my pleasure to thank all the respectable investigators of this study, and consequently the respective authors of the paper, for their remarkable efforts to carry out such difficult type of important clinical studies in the current era of deadly COVID-19 and the surrounding severe situation worldwide due to the pandemic.

The assessment of riskiness degree of the airborne exposure to SARS-CoV-2 in closed and indoor environments is still a debatable and questionable matter which needs much more accurate research and evidence-based discussions. As a good step to contribute in solving this debate and controversy, a small Italian research study was done at the Geriatric ward of a single hospital in Trieste (Italy) at mid-2020 to assess the applicability of airborne SARS-CoV-2 RNA monitoring, detection, and concentration measurement in healthcare indoor settings as an effective method for determining the infectivity of the air samples collected in indoor environment at risk due to the presence of COVID-19 patients. The main finding presented in this study is the possibility of transmission of COVID-19 infection among people through airborne SARS-CoV-2 particles.

After a primary logic and careful review of the titled paper, we can put a number of important concerns and issues with this study from my point of view, which include the following:

1. The sample size and specimens for the study (e.g., only 12 patients) is extremely small to give strong dependable results.
2. The study results lack enough degree of adequate generalizability, as the study was performed in only one small ward of one hospital in an Italian city.
3. The study model was not well designed, since it mainly based on expectations rather than facts.
4. The study designers did not put into consideration the expected emergence of continuous mutations of the SARS-CoV-2 genome when they carried out this clinical study in 2020, since they put the final conclusions with neglection to the future variations in the coronaviral-2 RNA and the possible evolution of diverse variants of the virus (which has been already occurred at the end of 2020 and continued up to

date at the end of 2021).

5. The study designers did not properly control for possible confounders and did not specifically enumerate or mention the different conditions with respect to the study main setting (the Geriatric ward) to provide the readers and clinical researchers with enough information and data to enable deep understanding of the situation and precise reproducibility of the results in the actual clinical practice, respectively.
6. The absence of the respective full data, e.g., gender, age, and demographic origin, of the 12 enrolled COVID-19 patients rendered the study results somehow misleading and not adequately representative.
7. The study investigators/paper authors did not accurately update the *in vitro* SARS-CoV-2 assay (which is used mainly for estimation of the RNA copies in their study) according to the latest modifications published online (before they published their paper) and they did not even cite the respective papers which reported these slight changes.[1][2] Even the *in vitro* SARS-CoV-2 assay in these respective papers was again slightly modified by newer papers at the last months of 2021.[3]
8. There is a time interval gap of about one year between the study time and the publication time of its relevant paper. During this period tens of concepts, theories, and facts about COVID-19 and the transmission/infection pathways of its virus (SARS-CoV-2) were changed and replaced by other new ones, thus the study results in this paper lack a significant degree of novelty in the current time.
9. Air monitoring in this study was short-term monitoring, thus it did not provide uninterrupted complete data to be suitable for overall evaluation.
10. The paper authors did not sufficiently discuss the study limitations in details in the Discussion section of the paper, and consequently they also did not put suitable suggestions for the possible solutions for these unraised limitations and issues in next planned studies in the very near future.

Finally, I hope that this simple critical mini-review can help the respected authors of this good-quality paper to improve this published paper in all possible ways (e.g., in an updated version of the paper), including addressing issues like the quality of the study model, updating of concepts/facts, and accuracy of results. I wish all the respective authors of this paper, which I had the chance to professionally review it, best of luck in their scientific journey and in all the coming publications that they will provide to the clinical medical research communities worldwide.

References

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