Seroconversion rate and diagnostic accuracy of serological tests for COVID-19

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Dear Editor,

We read the recent article by Zhao J et al which studied the antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019 [1]. This study is the need of the hour which might help in planning the testing strategy for COVID-19 in many countries. The study provided valuable information about immunological response in hosts, diagnostic accuracy of antibody assays and RT-PCR in diagnosing COVID 19. The findings of the study are very crucial in understanding the natural history of disease. However we have few concerns regarding the study.

First, in methodology it was mentioned that all enrolled participants were confirmed to be infected with SARS-CoV-2 by RT-PCR. However in results, the authors have mentioned that only 112 out of 173 participants tested positive for RNA over complete duration of the study, which contradicts the methodology. This finding raise the question about what was the gold standard test considered if not RT-PCR since RT-PCR is the gold standard test for COVID-19.

Second, in table 2, the sensitivity of RNA+Ab was calculated as 78.7% (74/94) during one to seven days after symptom onset. Denominator was considered to be 94 whereas only 87 participants have undergone RT-PCR and the same issue is repeated in all the time periods.

Third, Antibody tests in this study population should be interpreted cautiously since 1) there is plausibility to have cross reaction to antibodies related to other corona virus strains and 2) also diseases caused by other corona virus present with similar symptoms as COVID-19, and symptomatic patients might have antibodies which may lead to increased false positivity rate. Therefore present study should carefully interpret the serological tests and sensitivity should be calculated only in participants tested positive for RNA.

Fourth, the study reported that median duration for seroconversion was 11 days. However, this should be interpreted cautiously since nearly half of the participants were tested for antibody only after 8 days. It is not clear about whether all participants who tested positive for antibody have

given their first sample to be tested for antibodies, before 11 days (25% of them given first sample after 10 days). If not, the results might be biased. To reinforce this point, figure 2B shows that around 58% of the participants were positive for antibodies on day 8 and increased afterwards. With first assumption of Kaplan Meier method (censored participants will have same probability of experiencing event as uncensored), median time for seroconversion might be lesser than reported [2].

We would also like to know the clinical outcomes of the patients who had undetectable RNA in respiratory samples and had detectable antibodies in antibody assay since they could be cured of the disease and recovered with undetectable RNA. If all of the participants tested positive for antibody in later stages and negative for RNA, were declared as cured and discharged, serological tests will have negligible role in management of such cases in later stage.

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