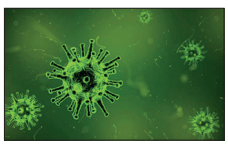
SARS-CoV-2: virus dynamics and host response



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Since December, 2019, coronavirus disease 2019 (COVID-19) has affected more than 100 000 patients globally.[1] COVID-19 is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and has a case-fatality rate of 2·3%, with higher rates among elderly patients and patients with comorbidities.[2] Person-to-person transmission is efficient, with multiple clusters reported. Clinically, patients with COVID-19 present with respiratory symptoms, which is very similar to the presentation of other respiratory virus infections. Radiologically, COVID-19 is characterised by multifocal ground-glass opacities, even for patients with mild disease.[3]

Knowledge of virus dynamics and host response are essential for formulating strategies for antiviral treatment, vaccination, and epidemiological control of COVID-19. However, a systematic study on these aspects has not been done. In *The Lancet Infectious Diseases*, Kelvin To and colleagues[4] report the viral load and antibody profiles of a cohort of 23 patients admitted to hospital with COVID-19. In these patients, the viral load peaked during the first week of illness then gradually declined over the second week. Viral load was also shown to correlate with age. Furthermore, both IgG and IgM antibodies started to increase on around day 10 after symptom onset, and most patients had seroconversion within the first 3 weeks. Finally, the IgG and IgM antibody level against the SARS-CoV-2 internal nucleoprotein and the surface spike receptor binding domain correlated with neutralising activity.

These findings have several practical implications. First, the high viral load during the early phase of illness suggests that patients could be most infectious during this period, and it might account for the high transmissibility of SARS-CoV-2. Furthermore, the high viral load on presentation suggests that SARS-CoV-2 could be susceptible to emergence of antiviral resistance. Second, age was associated with viral load in this study, which could explain the high degree of severe disease in older patients with SARS-CoV-2.[5,6] The high viral load in elderly patients is associated not only with low immunity but also with high expression of the ACE2 receptor (the cell-entry receptor for SARS-CoV-2) in older adults.[7] The timing of antibody seroconversion is crucial for determining the optimum timepoints for collecting serum specimens for antibody testing for diagnosis. Furthermore, this information is important for immunologists to choose the best timepoints for obtaining peripheral blood B cells for development of therapeutic monoclonal antibodies.[8]

The major strength of the study by To and colleagues is the systematic analysis of the serial viral load and antibody profile for up to 4 weeks, which provides insights into viral and host interactions during the acute and convalescent phases. Another notable aspect is that self-collected posterior oropharyngeal saliva samples were used, instead of nasopharyngeal specimens, for viral load monitoring. Collection of nasopharyngeal specimens is an invasive procedure, and it is uncomfortable for the patient and poses an infection risk to health-care workers. Self-collected saliva is much more acceptable to patients and is safer for health-care workers. This study clearly shows the feasibility of using saliva for viral load monitoring.

The information provided by To and colleagues is solid scientific evidence on COVID-19 for clinicians and scientists. Nonetheless, many questions are still outstanding on the viral characteristics and host response during infection. SARS-CoV-2 has been detected in faeces, blood, and urine samples,[9,10] and it is important to ascertain viral load dynamics in such samples, for prevention and control of the pandemic. Furthermore, the relation between viral load and disease severity needs to be further clarified. Studies with a larger sample size are needed to understand how different factors can affect viral load or antibody response. For example, immunocompromised patients might have higher viral load, prolonged viral shedding, and impaired antibody response. Future studies in the paediatric population are vital, because children seem to have much milder disease than in adults. Finally, a more detailed understanding of the innate and adaptive immune response against SARS-CoV-2 is important for understanding the pathogenesis and for designing vaccines.

We declare no competing interests.

*Yu Chen, *Lanjuan Li*
ljli @zju.edu.cn

State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, National Clinical Research Centre for Infectious Diseases, Collaborative Innovation Centre for Diagnosis and Treatment of Infectious Diseases, First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou 310003, China

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