

Clinical and Immunological Assessment of Asymptomatic SARS-CoV-2 infections

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Increasing evidence suggests that transmission of SARS-CoV-2 by presymptomatic or asymptomatic individuals likely contributes significantly to the COVID-19 pandemic.

Long et al¹ report the findings of a prospective observational case-control study conducted in Wanzhou District, China, which included 37 asymptomatic, RT-PCR confirmed hospitalized COVID-19 patients with close contact to known COVID-19 patients, identified by contact tracing. Based on the number of cases tracked by the local CDC surveillance system, asymptomatic infections constituted 20.8% of the total COVID-19 cases.

There are several important findings illustrated by this study; although asymptomatic patients appear to have similar initial viral loads (assessed by RT-PCR cycle threshold values) compared to symptomatic patients, the duration of viral shedding (interval between first to last positive nasopharyngeal swab) was significantly longer in the former group (19d vs 14d, $p = 0.03$). IgG levels were significantly higher in symptomatic patients for 2-3 months post infection, suggesting a more robust immunological response likely aiding virological clearance. While IgG levels gradually declined in both groups over this period, interestingly, 40% of the asymptomatic patients became seronegative for IgG compared to only 13% of the symptomatic patients. Unlike previous studies that have shown circulating antibodies to SARS-CoV and MERS-CoV for at least a year, these findings raise concern for a lower strength and duration of immunity in asymptomatic patients, increasing their risk for reinfection and eventual breakdown of herd immunity. Similar findings with respect to neutralizing antibodies have also been reported by Choe et al² in a small case-control study of 7 asymptomatic patients.

The study has a few limitations; the proportion of asymptomatic infections is likely overestimated as they were identified in a high-risk group of close contacts as opposed to a random population sample. Viral shedding was assessed on the basis of a positive RT-PCR of the nasopharyngeal swab - detection of viral RNA doesn't necessarily imply viable infectious virus. Lastly and more importantly, it is unknown if circulating IgG and neutralizing antibodies are truly representative of the strength of the adaptive (both B cell and T cell) immune response to SARS-CoV-2.

Critical knowledge gaps exist with respect to the incidence of asymptomatic infections and their immunological response. While this study provides some insight and raises concerns for reinfection, there is a need for larger longitudinal serological studies with rigorous methodologies to further validate these findings.

¹Long, Q., Tang, X., Shi, Q. *et al.* Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. *Nat Med*(2020). <https://doi.org/10.1038/s41591-020-0965-6>

²Choe PG, Kang CK, Suh HJ, Jung J, Kang EK, Lee SY, et al. Antibody responses to SARS-CoV-2 at 8 weeks postinfection in asymptomatic patients. *Emerg Infect Dis.* 2020 Sep [*date cited*]. <https://doi.org/10.3201/eid2610.202211>