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Letter to the Editor

Low transmission risk of 9 asymptomatic carriers tested positive for both SARS-CoV-2 nucleic acid and serum IgG

Dear Editor,

We read with interest a recent prospective contact-tracing study in this Journal by Huang et al.1, who reported a rapid asymptomatic transmission of COVID-19 during the incubation period demonstrating strong infectivity in a cluster of youngsters aged 16–23 years outside Wuhan. The COVID-19 pandemic has affected millions of lives worldwide partly due to its high contagiousness.2-3 Thus far, the growing amount of evidence suggests that asymptomatic carriers are capable of transmitting SARS-CoV-2.4-5 Here, we report clinical characteristics of nine confirmed COVID-19 asymptomatic carriers, who were tested positive both for SARS-CoV-2-specific nucleic acid and IgG, but appeared to be unable to transmit the virus.

Of 4973 SARS-CoV-2 nucleic acid positive results in Union hospital, Wuhan throughout the COVID-19 outbreak (from January 28, 2020 to May 12, 2020), we found nine asymptomatic carriers who were tested positive both for SARS-CoV-2-specific nucleic acid and IgG between March 28 and May 12, 2020. The SARS-CoV-2 nucleic acid was tested using throat swab specimens through real-time PCR (RT-PCR) to amplify the ORF1ab gene and N gene of SARS-CoV-2 (BioGerm, Shanghai, China). The primers for ORF1ab gene and corresponding detecting products: forward primer 5′-CCCTGTGGGTTTACACTTAA-3′, reverse primer 5′-ACGATTGCTACAGCTGA-3′, fluorescence probe 5′-FAM-CCCTGTGGGTTTACACTTAA-BHQ1-3′; for N gene and corresponding detecting products, forward primer 5′-GGCGAACTTCTCTGCTGAAAT-3′, reverse primer 5′-CAGACATTATTTGCTCAGCTG-3′, fluorescence probe 5′-FAM-TTGTCCCTGCTGACAGATT-TAMRA-3′. If the cycle threshold (Ct) value < 35 (or > 35 but less than 40 for two times), the specimens are defined as positive. Specific IgG against SARS-CoV-2 was detected using commercially available kit (#C86095G, YHLO biotechnology Co., LTD, Shenzhen, China) in an iFlash 3000 chemiluminescent immune analyzer (YHLO biotechnology Co., LTD, Shenzhen, China) through chemiluminescent microparticle immunoassay. This study was reviewed and approved by the Medical Ethical Committee of Union Hospital, Tongji Medical College, Huazhong University of Science and Technology.

Nine confirmed asymptomatic carriers who were tested positive for both SARS-CoV-2-specific nucleic acid and IgG (Patient 1–3 positive for IgG and IgM, and the others positive for IgG but negative for IgM) were retrospectively analyzed (Fig. 1). These patients were enrolled from outpatient population or general population requesting regular physical check-up. They have an average age of 47y (range 18–77y), five of which were male and four were female. Only one of them had comorbidity (Patient 8 with hypertension and diabetes). None of them received chest CT probably because of their lack of COVID-19 associated symptoms (Table 1). Two patients (Patient 1 and 3) were subject to in-hospital quarantine for 29 days, and then discharged because SARS-CoV-2 nucleic acid testing turned negative; the others remained quarantined in hospitals at the time of follow-up on May 12, 2020. The average Ct value of SARS-CoV-2 nucleic acid testing in nine patients were 36.42 ± 2.06 (ORF1ab gene, range 31.27–38.89) and 34.87 ± 3.73 (N gene, range 27.30–39.47). From the moment of Wuhan City lockdown (January 23, 2020) to the time of being admitted for quarantine, all these patients had lived together with their family members for an average of 85 days (range 65–104 days). All these patients developed no symptoms associated with COVID-19 during their quarantine. Of note, none of the patients’ close contacts (including all their family members who stayed with them) were RT-PCR tested positive for SARS-CoV-2, indicating they are not infected by these asymptomatic carriers despite of close contact.

We observed a small group of asymptomatic carriers (positive for both SARS-CoV-2-specific nucleic acid and IgG) with very low transmission risk. Our observation is consistent with a recent report suggesting that low transmission risk in asymptomatic patients.6 Such a low transmission risk might be partly associated with relatively high Ct values. This is in accordance with the observation that compared with severe COVID-19 cases, significantly lower viral loads were found in mild COVID-19 patients.7 The other possible reasons for low transmission risk: (1) the infectivity of the virus might be decreased in these confirmed asymptomatic carriers; (2) viral shedding might be ineffective without relevant symptoms, such as sneezing and coughing, thus reducing the risk of infections for close contacts.8

The analysis of this group of patients suggests that some asymptomatic carriers can be tested positive for SARS-CoV-2-specific nucleic acid and serum IgG, but they are of low transmission risk, which is different from previously-reported asymptomatic carriers, suggesting a new pattern may have emerged in SARS-CoV-2 infected patients and changes associated with viral load and virus infectivity. These have not been reported thus far.

However, close monitoring of the asymptomatic patients is still required. This work was limited in several aspects: (1) the sample size is limited (n = 9); (2) further investigation such as virus isolation and culture would strengthen the study, but we are unable to provide the results at this point, given current limited medical resources and urgent situations. The findings of this work may provide useful information for helping improve understanding and management of asymptomatic carriers and facilitating restoration of normal medical services after COVID-19 pandemic.

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Timeline of Nine Asymptomatic Carriers with SARS-CoV-2-Specific IgG Positive.
- Positive for SARS-CoV-2 nucleic acid testing.
- Negative for SARS-CoV-2 nucleic acid testing.
- IgG and IgM of anti-SARS-CoV-2 antibodies testing
- Admission
- Discharge

Fig. 1. Timeline of nine asymptomatic carriers with SARS-CoV-2-specific IgG positive.

| Table 1 Characteristics of nine asymptomatic carriers with SARS-CoV-2-specific IgG positive. |
|------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|
| Sex                                | Patient 1 Male | Patient 2 Female | Patient 3 Female | Patient 4 Male | Patient 5 Female | Patient 6 Male | Patient 7 Female | Patient 8 Male | Patient 9 Male |
| Age                                | 58y            | 56y              | 52y              | 42y            | 30y              | 18y              | 77y              | 38y              |
| Underlying diseases                | No             | No               | No               | No             | No               | No               | No               | Hypertension, diabetes |
| Initial symptoms associated with COVID-19 | No            | No               | No               | No             | No               | No               | No               | No               |
| CT evidence of pneumonia          | NA             | NA               | NA               | NA             | NA               | NA               | NA               | NA               |
| Date of positive for initial SARS-CoV-2 nucleic acid testing | Apr 13 | Mar 29 | Apr 10 | Apr 24 | Apr 13 | Apr 23 | Mar 28 | Apr 22 |
| CT value of ORF1ab gene for initial SARS-CoV-2 nucleic acid testing | 37.8 | 36.6 | 36.7 | 36.5 | 37.9 | 35.3 | 36.8 | 31.3 |
| CT value of N gene for initial SARS-CoV-2 nucleic acid testing | 37.5 | 37.7 | 27.3 | 36.4 | 39.5 | 34.0 | 35.0 | 29.9 |
| Date of initial testing for SARS-CoV-2-specific IgG and IgM | Apr 13 | Mar 29 | Apr 10 | Apr 24 | Apr 13 | Apr 23 | Mar 14 | Apr 22 |
| Result of initial testing for SARS-CoV-2-specific IgG and IgM | IgG (+), | IgG (+), | IgG (+), | IgG (+), | IgG (+), | IgG (+), | IgG (+), | IgG (+), |
| Date of admission                  | Apr 13 | Mar 29 | Apr 10 | Apr 25 | Apr 13 | Apr 24 | Mar 28 | Apr 22 |
| Date of negative for initial SARS-CoV-2 nucleic acid testing | Apr 26 | May 10 | Apr 26 | May 2 | Apr 27 | Apr 28 | Apr 5* | Apr 28 |
| Date of discharge                  | May 12 | NA**          | May 9          | NA**          | NA**          | NA**          | NA**          | NA**          |
| Symptoms associated with COVID-19 during quarantine | No             | No               | No               | No             | No               | No               | No               | No               |
| Days for patients living with their family members since Jan. 23, 2020 (Wuhan lockdown) | 81             | 104              | 78               | 93             | 81               | 92               | 65               | 90               |
| The status of SARS-CoV-2 nucleic acid testing for all close contacts | Negative | Negative | Negative | Negative | Negative | Negative | Negative | Negative |
Author contributions

All authors participated in design, collected and analyzed data, drafted the manuscript and approved the final submitted version. Chen, Fu, and Yang contributed equally to the work.

Declaration of Competing Interest

The authors declare no conflicts of interest.

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