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COMMENTARY

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Asymptomatic cases with SARS-CoV-2 infection

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Abstract

On 31 March 2020, Chinese Health Authorization announced that numbers of asymptomatic cases with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection will be made to the public daily. This was a very important step since different counties have different capacities for the detection of SARS-CoV-2 infection and control strategy for the Coronavirus Disease 2019 outbreak. We summarized the characteristics of asymptomatic SARS-CoV-2 infections and the transmission potential of asymptomatic cases. Then we provided guidelines for the management of asymptomatic cases through quarantine and nucleic acid/serology tests.

KEYWORDS

coronavirus, epidemiology, horizontal transmission, pathogenesis, respiratory tract, SARS coronavirus, virus classification

1 | INTRODUCTION

The outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become a global pandemic. Till 31 March 2020, there were more than 82 600 confirmed cases in the mainland China and 855 000 cases worldwide, leading to over 42 000 cases of death, causing heavy economic loss and continually threatening life safety. The infection with SARS-CoV-2 seems to spread more easily than other diseases, including seasonal influenza. Calculations of R0 (the number of people on an average one infected person will pass on the virus) suggest a range of 2 to 2.5.[1] Coronavirus Disease 2019 (COVID-19) cases in China stared rapid decline in March, COVID-19 cases or cases with SARS-CoV-2 infections slowly increased in a few countries (South Korea and Japan), while these cases have been rapidly increasing in most countries worldwide. On 31 March 2020, Chinese Health Authorization announced that numbers of asymptomatic cases with SARS-CoV-2 infection will be made to the public daily. This was a very important step since different counties have different capacities for the detection of SARS-CoV-2 infection and control strategy for the COVID-19 outbreak. We summarized in this article how asymptomatic COVID-19 cases have been screened and managed in China.

2 | WHAT IS ASYMPTOMATIC INFECTION?

Recently, "asymptomatic infection," also known as "hidden coronavirus infections" (https://www.sciencemag.org/news/2020/02/labs-scramble-spot-hidden-coronavirus-infections#) or "covert coronavirus infections" (https://www.nature.com/articles/d41586-020-00822-x) have been given public concerns, researchers began to dig into the underlying infectiousness of the asymptomatic infected patients. Asymptomatic carrier refers to patients who have mild or non-symptoms but with a positive test for the viral nucleic acid of SARS-CoV-2 or with a positive test for serum specific immunoglobulin M antibody (National Health Commission of the People's Republic of China. COVID-19 prevention and control Protocol [6th edition] 2020; http://www.nhc.gov.cn/jkj/s3577/202003/4856d5b0458141fa9f376853224d41d7.shtml).

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There are two classes of asymptomatic cases with SARS-CoV-2 infection: first, cases with little or mild symptoms within the incubation period but with symptoms onset in the coming 14-day quarantine period or typical changes on the chest-radiograph. The other refers to the patient with no symptoms all the time but tested positive for viral nucleic acid or antibodies.

Asymptomatic cases are often screened for close contacts both in the clinic and in community, such as cohabiting family members of COVID-19 patients or suspected patients or individuals who have exposed to COVID-19 patients within a short distance and relatively long time. Other circumstances include screening for clustering occurrence or tracing the source of infection.

Currently, asymptomatic cases are not included in the confirmed patients in everyday-report according to the "Novel Coronavirus Pneumonia Diagnosis and Treatment Protocol (7th edition, trial)." Once found, the patient will be put into medical isolation for up to 14-days, if the patient has symptoms onset within the isolation period, he/she will be reported as a confirmed case immediately.

3 | HOW MANY ASYMPTOMATIC CASES?

Evidence is accumulating on the existence of many asymptomatic or presymptomatic cases. On 5 February 2020, a Japan cruise ship called the Diamond Princess hosting 3711 people underwent a 2-week quarantine after a former passenger was found with COVID-19 after debarking (National Health Commission of the People's Republic of China. Novel coronavirus Pneumonia Diagnosis and Treatment Protocol [5th edition, trial] 2020; http://www.nhc.gov.cn/yzygj/s7653p/202003/46c9294a7dfe4cef80dc7f5912eb1989.shtml). Until 20 February, 634 persons onboard tested positive for SARS-CoV-2. Of the 634 confirmed cases, a total of 306 and 328 were reported to be symptomatic and asymptomatic, the asymptomatic proportion was 50.5% (320/634). The asymptomatic cases reported in the article consists of both true asymptomatic cases with SARS-CoV-2 infection and cases who had not yet developed symptoms at the time of data collection but became symptomatic later. As predicted using a statistical model, the estimated total number of true asymptomatic cases was at 113.3 and the estimated asymptomatic proportion (among all infected cases) was 17.9%. Another study reported that the asymptomatic ratio was estimated at 30.8% among evacuees tested positive for SARS-CoV-2 using the information on Japanese nationals that were evacuated from Wuhan, China.[2] In this study, the length of observation was long enough to cover the COVID-19 incubation period.[3,4] A recent study reported a familial cluster with three asymptomatic cases. Studies from single-center reported 4% to 6% cases with SARS-CoV-2 did not develop any symptom during the course of the disease.[5,6] Thus, there is very little probability that the virus-positive asymptomatic individuals will develop symptoms later, the ratio is slightly smaller than that of influenza, which was estimated at 56% to 80%. Recently, a preprint published on medRxiv analyzed the evolving epidemiology before and after nonpharmaceutical interventions put into effect using an SEIR model. The study indicated at least 59% of infected cases were unascertained in Wuhan which included both asymptomatic and mild-symptomatic cases. The study further assumed if no unascertained cases in the initial state, the estimated cases would be much lower on 23 and 25 January. Besides, there would be about 2 weeks delay in the predicted ending date of the epidemic when taking the unascertained cases into account. Therefore, substantial unascertained cases have important implications for the evaluation and control of the COVID-19 epidemic.

4 | CAN ASYMPTOMATIC CASES SPREAD VIRUSES?

With the extension of the epidemic trend of COVID-19, more and more researchers begin to question about the contagious capacity of these asymptomatic cases. On 21 February 2020, JAMA reported the first case of transmission of SARS-CoV-2 from an asymptomatic carrier with normal chest computed tomography findings.[7] Five family members were most likely been infected by one asymptomatic family member who lives in Wuhan and traveled to Anyang on 10 January 2020. The event suggests that SARS-CoV2 may have been transmitted by the asymptomatic carrier for the first time. Later on, in a study described the demographic and clinical features of 24 asymptomatic patients in Nanjing, China, seven cases showed normal computed tomography (CT) images and had no symptoms from beginning to the end.[7] Strikingly, through epidemiological investigation, researchers observed a typical asymptomatic transmission to the cohabiting family members, which in the most serious case even caused severe COVID-19 pneumonia. One recent research focused on the epidemiological characteristics of pediatric patients with COVID-19, and found over 90% of all pediatric patients were asymptomatic, mild, or moderate cases, the clinical manifestation of children's COVID-19 cases were generally less severe than those of adults' patients, thus, children infected with COVID-19 were more likely of being asymptomatic cases.[11] There is no evidence on asymptomatic children as potential infection sources since most children have relatively few opportunities to expose themselves to pathogens or sick patients, and were usually infected by other family members. In a study assessing viral loads of different time points and samples providing proof of active virus replication in upper respiratory tract tissues.[12] Pharyngeal virus shedding was very high during the first week of symptoms. The virus can be detected at a very early stage of the disease when symptoms are relatively mild or in the prodromal stage, suggesting a more efficient transmission of SARS-CoV-2 through active pharyngeal viral shedding at a time when symptoms are still mild. Another study monitored SARS-CoV-2 viral loads in upper respiratory specimens obtained from 18 patients including one patient who never developed symptoms along with unremarkable CT scan findings.[13] The asymptomatic patient's nasal swabs and throat swabs tested positive on days 7, 10, and 11 after contact. The viral load detected in the asymptomatic patients was similar to that in the symptomatic patients, suggesting the transmission potential of asymptomatic or minimally symptomatic patients. One study reported that an asymptomatic case

tested for positive in feces, but not in nasopharyngeal swabs, suggesting the possibility of transmission via fecal-oral route.[14]

5 | THOUGHTS ON THE INFECTIVITY OF ASYMPTOMATIC CASES IN REAL WORLD

Although grooming evidence suggest possible transmission of SARS-CoV-2 from asymptomatic cases, the World Health Organization declared that coronavirus has relatively low risk transmitted through asymptomatic cases from past experience in the middle east respiratory syndrome. Asymptomatic cases are unlikely the major driver of transmission in COVID-19, otherwise, more cases of infection would have been presented.

Besides, the process of viral shedding of asymptomatic patients is limited by the lack of symptoms such as coughing and sneezing, reduced the risk of infection. The relatively low viral loads of asymptomatic patients also limit their capacity of transmission and being the so-called super-spreader. Testing positive for viral nucleic acid is subjected to viral loads and activity, thus, physicians should be cautious in interpreting the result of the viral nucleic acid test. Status of "Living/dead" of the virus should be taken into consideration.

6 | MANAGEMENT OF ASYMPTOMATIC CASES

According to "COVID-19 prevention and control Protocol (6th edition)," asymptomatic patients should be quarantined and monitored for 14 days, quarantine ends when two consecutive samples of the nucleic acid test showed negative (the interval between sampling should be more than 24 hours) (National Health Commission of the People's Republic of China. COVID-19 prevention and control Protocol [6th edition] 2020). Two writers advocated the application of antibody tests which might help screen different age groups of humans to determine how many people become infected with few or no symptoms and illuminate the actual rate of confirmed cases (https://www.sciencemag.org/news/2020/02/labs-scramble-spot-hidden-coronavirus-infections#. https://doi.org/10.1126/science.abb2651).

7 | CONCLUSION

With the existence of disagreement in the actual number of asymptomatic cases and their infectivity, larger observational studies including serological tests with a longer period are needed.[15] Currently, for asymptomatic patients to follow strict quarantine is of great importance in the control of the COVID-19 epidemic. If various feasible measures are taken to control the transmission, then the outbreak could be ended as soon as possible.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

YW and HK contributed equally to this work. Conception or design of the work: YW, HK, ZT. Data collection: YW, HK. Drafting the article: YW, HK. Critical revision of the article: ZT, XL. Final approval: YW, HK, XL, ZT.

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