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Short Communication

Duration of viral shedding in asymptomatic or mild cases of novel coronavirus disease 2019 (COVID-19) from a cruise ship: A single-hospital experience in Tokyo, Japan

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ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is the cause of novel coronavirus disease 2019 (COVID-19), was first reported in Wuhan, China, and now has spread across the world as a global pandemic. The propagation from asymptomatic polymerase chain reaction (PCR)-positive individuals represents a complicating factor in the efforts to control the COVID-19 pandemic. We examined the course of PCR assays and the duration of viral shedding in 23 asymptomatic or mild COVID-19 patients from the cruise ship who were admitted to our hospital. Among these 23 cases, the median duration of viral shedding was 19 days (range, 6–37 days) from initial viral detection. Eight cases (35%) had another positive PCR result after testing negative once. Although the duration of viral shedding was approximately three weeks, the infectivity and transmissibility period from asymptomatic and mild COVID-19 cases is unclear. Further studies are needed to determine how long such asymptomatic and mild COVID-19 cases have infectivity.

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The novel coronavirus (severe acute respiratory syndrome coronavirus 2; SARS-CoV-2), which is the cause of novel coronavirus disease 2019 (COVID-19), first reported in Wuhan, China, has spread across the world and has been characterized by the World Health Organization as a global pandemic (Bedford et al., 2020). In February 2020, at the port of Yokohama, Japan, an outbreak of COVID-19 among passengers and crew of the *Diamond Princess* cruise ship occurred, with approximately 700 confirmed cases. All patients, including those with asymptomatic and mild disease, were transferred to Japanese medical institutions, including our hospital for quarantine and treatment until viral shedding stopped (Kakimoto et al., 2020; Zhang et al., 2020). The information that can be gleaned from the results of polymerase chain reaction (PCR) assay about the time course of asymptomatic or mild COVID-19 is limited (Hu et al., 2020; Zhou et al., 2020). We report the sequence of PCR assays and the duration of viral shedding in 23 asymptomatic or mild COVID-19 patients from the cruise ship who were admitted to our hospital.

We performed a retrospective review of 25 laboratory-confirmed COVID-19 cases, whose oropharyngeal or nasopharyngeal swab

samples were positive for SARS-CoV-2 by quantitative reverse transcriptase PCR while at the government quarantine facility before admission to our hospital, and who were admitted to our hospital between February 18 and 25, 2020, when 25 cases disembarked. The median days from PCR assay to admission to our hospital were three days (range, 1–5 days). All cases received laboratory tests and chest X-ray on admission. PCR status was evaluated twice or more per week at the government quarantine facility, and the resolution of viral shedding is defined as two consecutive negative PCR tests on oropharyngeal or nasopharyngeal swab samples. In cases with re-positive PCR results, the resolution of viral shedding is defined as those after the re-positive PCR test. Mild illness was defined as non- and mild pneumonia without dyspnea, tachypnea, and hypoxemia (Wu and McGoogan, 2020). Because two cases were transferred to tertiary care hospitals after a few days due to concerns about the severity of their pneumonia from initial chest computed tomography (CT), 23 patients were evaluated for viral shedding. To explore the factors associated with viral shedding, univariate analysis was performed using the Mann-Whitney U test for continuous variables, or Fisher's exact test for categorical variables. The following factors were taken into consideration: age, sex, comorbidities (Gandhi et al., 2020), body temperature (BT) and peripheral oxygen saturation (SpO₂) on admission, highest recorded BT and lowest SpO₂ during hospitalization, presence of symptoms, laboratory results (white blood cell count, lymphocyte count, lactate dehydrogenase, blood

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urea nitrogen, serum creatinine, and C-reactive protein), and imaging findings.

The characteristics of the 23 cases are shown in Table 1. Among them, ten cases were Japanese, six were Australian, two each were American and Indonesian, and one each was Canadian, Thai, and Romanian. Cases ranged in age from 29 to 79 years (median age 67 years), and 13 (52%) had comorbidities such as hypertension, diabetes mellitus, or coronary heart disease. Fifteen patients were asymptomatic, and eight had very mild symptoms that improved with symptomatic treatment. Chest CT was performed on two patients with suspected pneumonia findings on chest X-ray at admission to our hospital, and multiple ground-glass opacities (GGOs) were found in two patients (Case 13 and 17). The remaining 21 cases had no imaging findings by chest X-ray. Recordings of PCR results for all patients are shown in Figure 1. In one month of follow-up, viral shedding resolved in 21 cases, and the remaining two cases (Case 1 and 2) took 37 days to resolve. Case 1 is a previously healthy 30-year-old man who had a low-grade fever (37.5 °C) on admission without other obvious symptoms. Case 2 is a 57-year-old woman with a history of thyroid cancer, arrhythmia, and pulmonary thromboembolism. She had a mild headache during hospitalization. However, these two cases did not have any respiratory symptoms during hospitalization.

Eight cases (35%) (Case 1, 2, 3, 6, 8, 9, 10, and 11) had another positive PCR result after testing negative once. The median duration of viral shedding was 19 days (range, 6–37 days) from initial viral detection. Three (13%) non-Japanese cases (Case 10, 11, and 19) had two consecutive negative PCR results on oropharyngeal swab samples but were not able to go back to their country after discharge from hospital, because these cases needed

nasopharyngeal swab samples according to their national criteria. In univariate analysis, no clinical and laboratory factors were associated with PCR negativity by 14, 21, and 28 days from initial viral detection (Supplementary Table 1).

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Although approximately half of the 23 asymptomatic or mild COVID-19 cases had some comorbidities and 16 (70%) of the 23 cases were 60 years and older, all 23 cases did not develop severe symptoms and had no trouble with daily activities during hospitalization for COVID-19. Several studies have reported the clinical course of asymptomatic cases of COVID-19 (Hu et al., 2020; Zhou et al., 2020; Xu et al., 2020; Inui et al., 2020). Hu et al. reported that five of 24 patients were symptomatic during hospitalization, and 12 had GGOs on chest CT, and all cases improved without becoming severe (Hu et al., 2020). Inui et al. reported that of 82 asymptomatic COVID-19 cases disembarking from the *Diamond Princess* cruise ship, 44 (54%) had lung opacities on CT (Inui et al., 2020). In our cases, chest CT was performed only when pneumonia was suspected on a chest X-ray. Therefore, GGOs might be more common findings on chest CT in asymptomatic or mild cases.

Table 1
Characteristics of cases.

Characteristics	Value (n = 23)
Median age, years (range, interquartile)	67 (29–79, 56.5–70.5)
Age ≥60 years	16 (70%)
Sex	
Male	10 (43%)
Female	13 (57%)
Comorbidities	
Hypertension	5 (22%)
Dyslipidemia	5 (22%)
Diabetes	3 (13%)
Coronary artery disease	1 (4%)
Parkinson disease	1 (4%)
Nontuberculous mycobacteria	1 (4%)
Bronchial asthma	1 (4%)
Ulcerative colitis	1 (4%)
Old cerebral infarction	2 (9%)
Solid tumor	2 (9%)
Comorbidities associated with severe COVID-19 ^a	7 (30%)
Vital signs	
Median body temperature on admission, °C (range, interquartile)	36.6 (35.9–37.5, 36.2–36.9)
Median highest body temperature during hospitalization, °C (range, interquartile)	37 (36.6–37.6, 36.8–37.2)
Median peripheral oxygen saturation on admission, % (range, interquartile)	98 (96–99, 97–98)
Median lowest peripheral oxygen saturation during hospitalization, % (range, interquartile)	96 (90–98, 95–97)
Symptoms	
Cough	4 (17%)
Headache	2 (9%)
Sputum	1 (4%)
Fatigue	1 (4%)
Diarrhea	1 (4%)
None	15 (65%)
Laboratory findings	
Median white blood cell count, ×10 ⁷ /L (range, interquartile)	5820 (3930–10,230, 5040–7075)
Median lymphocyte count, ×10 ⁷ /L (range, interquartile)	1760 (590–2895, 1471–1970)
Median lactate dehydrogenase, U/L (range, interquartile)	185 (132–284, 163–218)
Median blood urea nitrogen, mg/dl (range, interquartile)	12.8 (7.9–12.8, 9.3–16.2)
Median serum creatinine, mg/dl (range, interquartile)	0.75 (0.38–1.18, 0.55–0.90)
Median C-reactive protein, mg/dl (range, interquartile)	0.17 (0.04–1.96, 0.11–0.46)

^a Gandhi et al. (2020).

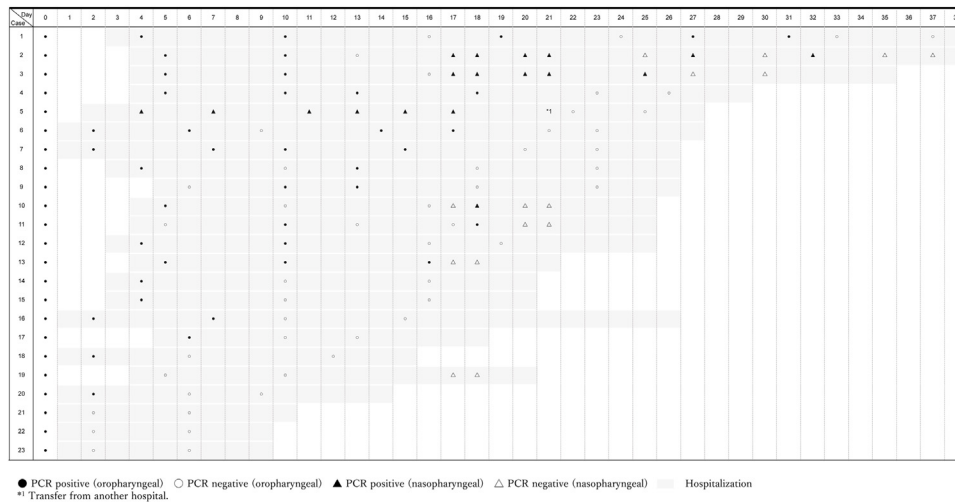


Figure 1. Time course of PCR assays of the 23 asymptomatic or mild infections with SARS-CoV-2 from the *Diamond Princess* cruise ship, Japan. The gray boxes indicate admission to our hospital for quarantine.

We experienced two cases (Case 1 and 2) that took 37 days after initial viral detection to become negative on PCR assay. Another study similarly reported that it took more than one month to achieve PCR negativity in asymptomatic patients (Zhou et al., 2020). Recent studies have reported transmission from asymptomatic PCR-positive individuals during this pandemic (Rothe et al., 2020; Bai et al., 2020; Yu et al., 2020). However, it is unknown how long asymptomatic PCR-positive individuals are contagious. Therefore, propagation from asymptomatic PCR-positive individuals represents a complicating factor in the efforts to control the COVID-19 pandemic. The discharge criteria for asymptomatic patients with COVID-19 in Japan are two consecutive negative PCR results, performed at least 48 h after the first PCR and repeated at least 12 h apart, which approximates the discharge criteria that have been established in China (Zhou et al., 2020; Xu et al., 2020). Our study showed the majority of specimens for PCR assay were derived from an oropharyngeal swab. However, the sensitivity to detect SARS-CoV-2 might differ from different types of specimens. Indeed, testing of nasal swab specimens was more sensitive than those of oropharyngeal swab specimens (Wang et al., 2020).

Moreover, false-negative results may occur regardless of types of specimens. All these findings might contribute to re-positive PCR results in our study. Further study is required whether re-positive cases are infective or not.

Given the World Health Organization's designation of COVID-19 as a pandemic, and that the number of infected patients is now increasing in Japan, the infectivity and transmissibility period from asymptomatic and mild COVID-19 cases must be ascertained. Quarantine of asymptomatic or mild COVID-19 cases in medical facilities will be helpful for pandemic control (Chen et al., 2020). Therefore, the optimal discharge criteria should be reconsidered as necessary for each affected area to ensure the proper allocation of limited medical resources.

Author's contributions

All authors participated in the care of the patients. KI wrote the first manuscript draft.

Conflict of interest

The authors declare no competing financial interests.

Ethical approval

This retrospective study was approved by the Institutional Review Board of our hospital.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.ijid.2020.06.020>.

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