

Suspected COVID-19 Reinfections at a Tertiary Care Center, Iowa, 2020

Dear Editor,

Reinfections with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been recently reported [1–5]. However, the rate of reinfections is difficult to determine because real-time reverse transcription polymerase chain reaction (RT-PCR) can detect SARS-CoV-2 RNA for weeks after infection [6] and criteria used to retest and define reinfections have varied. Moreover, use of viral whole-genome sequencing (WGS) to prove reinfection with new strains or clades [1–5] is not yet widely adopted. The Centers for Disease Control and Prevention (CDC) recently released a new coronavirus disease 2019 (COVID-19) reinfection investigation protocol with a time threshold of ≥ 45 days from the first episode and a cycle threshold (Ct) of < 33 [7]. We used the CDC investigation protocol to determine the rate of clinically suspected reinfections at the University of Iowa Hospitals & Clinics (UIHC; an 811-bed academic medical center) and confirmed 1 reinfection using whole-genome sequencing.

Patients with respiratory complaints underwent SARS-CoV-2 RT-PCR using nasopharyngeal swabs. During March–April 2020, the CDC 2019-nCoV-EUA-01 Diagnostic Panel (which uses 2 targets, N1 and N2 genes) was used; most subsequent samples were tested with the TaqPath RT-PCR COVID-19 Combo kit, which uses 3 targets (ORF1ab, S gene, N gene). We identified patients with laboratory-confirmed COVID-19 who underwent repeat RT-PCR ≥ 45 days from first positive test for new respiratory complaints. We identified patients with mean Ct values < 33 on repeat RT-PCR according to CDC investigation protocols for suspected reinfections. We performed WGS on 1 pair of available samples from

Table 1. Characteristics of Patients With Suspected COVID-19 Reinfections at a Tertiary Care Center, Iowa March–December 2020

Patient	Age	Sex	Comorbidities	1st Ct Value (ORF1ab, S, and N genes) or * (N1, N2 Genes)	2nd Ct Value (ORF1ab, S-gene, N-gene)	Symptoms on Second Presentation	Time Between 1st and 2nd Tests, d	Treatment for First Episode	Treatment for Suspected Reinfection	Outcome	WGS
1	18	Female	Asthma	26* (26, 26)	28 (29, 29, 25)	Cough, sore throat, malaise	75	None	None	Recovered	No
2	19	Female	None	28 (28, 29, 28)	22 (21, 22, 23)	Headache, nasal congestion, loss of taste and smell	63	None	None	Recovered	No
3	22	Female	None	24* (24, 23)	17 (16, 17, 17)	Headache, sore throat, cough, rash, fever	72	None	None	Recovered	Yes
4	23	Female	Morbid obesity	29 (30, 29, 29)	31 (32, 31, 31)	Cough	60	None	None	Recovered	No
5	25	Female	Morbid obesity	22* (22, 21)	24 (24, 24, 23)	Rhinorrhea, cough	94	None	None	Recovered	No
6	43	Female	AML, thyroid carcinoma, bone marrow transplant, graft-vs-host disease on chronic immunosuppressive therapy, scleroderma	17 (16, 17, 17)	19 (18, 21, 19)	Cough	134	None	Bamlanivimab	Recovered	No
7	44	Male	Morbid obesity, prediabetic, OSA	38 (40, 40, 35)	25 (24, 26, 25)	Nasal congestion, cough, rash, diarrhea, malaise	92	None	None	Recovered	No

Abbreviations: AML, acute myeloid leukemia; COVID-19, coronavirus disease 2019; Ct, cycle threshold; NA, not available; OSA, obstructive sleep apnea; WGS, whole-genome sequencing.

a suspected case to confirm reinfection (MinION sequencer, ARTIC network protocols); at least 1 sample from all remaining sample pairs had been discarded by the institution due to sample storage space limitations. This study was approved by the Institutional Review Board of the University of Iowa.

A total of 13 603 patients had a positive RT-PCR during March–December 2020; of these, 296 (2.2%) had new symptoms and an RT-PCR test repeated ≥ 45 days from the first test. Twenty-nine (0.2% of all patients) had a positive repeat RT-PCR. Four of these samples were tested with a respiratory viral panel distinct from TaqPath; these were removed from our analyses. Ct values were available for 25 of 29 patients; 7 cases (28% of positive repeat RT-PCR, 0.05% of total cohort) had Ct values < 33 on repeat RT-PCR (Table 1). The median age (range) was 23 (18–44) years, and most were women (86%). The median time to repeat test (range) was 75 (60–134) days. The mean Ct value on repeat test was 23.8 (16.6–31.0). The most common symptom for retesting was cough (86%). One patient with acute myeloid leukemia received bamlanivimab the second time. None required hospitalization. Specimens for WGS were available for 1 patient: A 22-year-old healthy woman presented with a 1-day history of headache, sore throat, and malaise. SARS-CoV-2 RT-PCR was positive. She fully recovered by day 14, with negative RT-PCR on days 16 and 17. Two months later, she developed sore throat, rash, and fever. COVID-19 RT-PCR was positive (Ct = 17). WGS confirmed 2 different clades in the first and second infections (20C and 20G). She recovered without specific treatment.

We summarized 7 possible COVID-19 reinfections according to the CDC

reinfection investigation criteria and confirmed 1 using WGS. One suspected reinfection in an immunosuppressed patient may have been a persistent infection [8]. Previously reported case series have not used a time threshold (≥ 45 days) or Ct values (< 33) [9, 10]. As a positive RT-PCR after recovery does not necessarily indicate reinfection, WGS can be used to further confirm the diagnosis. In addition, given the emergence of new variants, there is a greater role of WGS; however, WGS is not yet routinely available for clinical use. Reinfections could be subclinical and may not have been detected in our investigation; however, they could contribute to transmission. In conclusion, in patients with a recent history of COVID-19, recurrence of symptoms and a positive RT-PCR at least 45 days after the first diagnosis were rare (0.2%). Among them, only 1 in 4 (0.05% of the full cohort) had Ct values suggestive of reinfection/persistent infection, and none required hospitalization.

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