The Daily COVID-19 Literature Surveillance Summary

December 04, 2020

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COVID-19 Daily Literature Surveillance

COVID19LST

Bringing you real time, distilled information for guiding best practices during the COVID-19 pandemic

LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances**	Local non-random sample**	Case-series**	n/a
Is this diagnostic or monitoring test accurate? (Diagnosis)	Systematic review of cross sectional studies with consistently applied reference standard and blinding	Individual cross sectional studies with consistently applied reference standard and blinding	Non-consecutive studies, or studies without consistently applied reference standards**	Case-control studies, or "poor or non-independent reference standard**	Mechanism-based reasoning
What will happen if we do not add a therapy? (Prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort study or control arm of randomized trial*	Case-series or case-control studies, or poor quality prognostic cohort study**	n/a
Does this intervention help? (Treatment Benefits)	Systematic review of randomized trials or *n*-of-1 trials	Randomized trial or observational study with dramatic effect	Non-randomized controlled cohort/follow-up study**	Case-series, case-control studies, or historically controlled studies**	Mechanism-based reasoning
What are the COMMON harms? (Treatment Harms)	Systematic review of randomized trials, systematic review of nested case-control studies, *n*-of-1 trial with the patient you are raising the question about, or observational study with dramatic effect	Individual randomized trial or (exceptionally) observational study with dramatic effect	Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.)**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning
What are the RARE harms? (Treatment Harms)	Systematic review of randomized trials or *n*-of-1 trial	Randomized trial or (exceptionally) observational study with dramatic effect			
Is this (early detection) test worthwhile? (Screening)	Systematic review of randomized trials	Randomized trial	Non -randomized controlled cohort/follow-up study**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning

*** Level may be graded down on the basis of study quality, imprecision, indirectness (study PICO does not match questions PICO), because of inconsistency between studies, or because the absolute effect size is very small; Level may be graded up if there is a large or very large effect size.**

**** As always, a systematic review is generally better than an individual study.**

How to cite the Levels of Evidence Table

OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence".
Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653

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EXECUTIVE SUMMARY

Understanding the Pathology

- Investigators in South Korea analyzed samples from 6 COVID-19-positive patients at 3 tertiary hospitals who had recovered with negative SARS-CoV-2 rRT-PCR results and then presented again with subsequent positive rRT-PCR results. One of the patients, a 21-year-old female with allergic rhinitis, recovered with resolution of symptoms, then presented 2 additional times with mild symptoms and subsequent positive testing. A whole-genome sequencing from samples taken at her first and her third presentations found two distinct genomic clades between the viral RNA in the 2 samples, suggesting evolutions of the SARS-CoV-2 genome. Their findings suggest that SARS-CoV-2 infection may not confer immunity against subsequent reinfections of different strains, and precaution should continue to be taken even after recovery.

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ADULTS

CLINICAL FEATURES AND OUTCOMES OF PATIENTS WITH HUMAN IMMUNODEFICIENCY VIRUS WITH COVID-19

Gervasoni C, Meraviglia P, Riva A, Giacomelli A, Oreni L, Minisci D, Atzori C, Ridolfo A, Cattaneo D.. Clin Infect Dis. 2020 Nov 19;71(16):2276-2278. doi: 10.1093/cid/ciaa579.
Level of Evidence: 3 - Local non-random sample

BLUF

A retrospective observational study conducted by infectious disease specialists at ASST Fatebenefratelli Sacco University in Italy between February 21 and April 6, 2020 using the Department of Infectious Diseases database found HIV-positive patients admitted with COVID-19 (n=47; Table 1) were not at a significantly greater risk of death when given appropriate pharmacological therapy (2 deaths; Table 2) than HIV-negative patients with COVID-19. Authors hope to inform clinicians on HIV-status in COVID-19 patients, but they acknowledge a need for larger cohort studies to confirm these findings.

ABSTRACT

Little is known about the clinical outcomes of HIV patients infected with SARS-CoV-2. We describe 47 patients referred to our hospital between 21 February and 16 April 2020 with proven/probable COVID-19, 45 (96%) of whom fully recovered and two died.

FIGURES

Table 1.
Characteristics and Symptoms of Patients With Human Immunodeficiency Virus Infected With SARS-CoV-2

Clinical Features	Overall	Females	Males
Patients, n (%)	47	11 (23)	36 (77)
Age, mean ± SD, years	51 ± 11	53 ± 12	50 ± 11
CD4 cell count, mean ± SD, cells/mm^3	636 ± 290	658 ± 279	630 ± 296
Patients with HIV viral load <20 copies/mL, n (%)	44 (94)	11 (100)	33 (92)
Patients with at least 1 comorbidity, n (%)	30 (64)	9 (82)	21 (58)
Comorbidities per patient, mean ± SD, n	2.0 ± 1.0	1.9 ± 0.8	2.0 ± 1.0
Comorbidities, n			
Dyslipidemia	15	7	8
Hypertension	14	5	9
Hepatitis C or B coinfection	5	1	4
Renal disease	4	0	4
Diabetes mellitus	3	1	2
Epilepsy	2	0	2
Cardiovascular disease	2	1	1
Neoplasms	3	0	3
Gastritis	2	0	2
Organ transplantation	1	0	1
Chronic obstructive pulmonary disease	2	0	1

Symptoms at onset, n			
Fever	41	9	32
Cough	23	7	16
Dyspnea	10	3	7
Diarrhea	7	2	5
Myalgia	4	2	2
Headache	3	2	1
Time from onset to offset, mean ± SD, days	14 ± 8	11 ± 7	14 ± 9
Patients with SARS-CoV-2 testing, n (%)	28 (60)	6 (55)	22 (61)
PCR-positive test, n	26	6	20
IgG/IgM rapid test, n	2	0	2
Patients with risk factors for COVID-19, n (%)	21 (45)	6 (55)	15 (42)
Healthcare providers, n	6	3	3
Colleagues with COVID-19, n	4	0	4
Relatives with COVID-19, n	11	3	8
Hospitalized patients, n (%)	13 (28)	2 (18)	11 (31)
Chest CT–confirmed pneumonia, n (%)	12 (25)	2 (18)	10 (28)
Oxygen demand, n	4	1	3
Mechanical ventilation, n	2	0	2
Deaths, n	2	0	2
Fully recovered, n (%)	45 (96)	11 (100)	34 (94)

Abbreviations: COVID-19, coronavirus disease 2019; CT, computed tomography; HIV, human immunodeficiency virus; Ig, immunoglobulin; PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Table 1 continued. Characteristics and Symptoms of Patients With Human Immunodeficiency Virus Infected With SARS-CoV-2

Table 2.
Pharmacological Treatments of Patients With Human Immunodeficiency Virus Infected With SARS-CoV-2

Drugs	Overall (N = 47)	Females (n = 11)	Males (n = 36)
COVID-19 therapies			
Paracetamol	25	5	20
Hydroxychloroquine	8	3	5
Azithromycin	7	3	4
Other antibiotics	6	1	5
Lopinavir/ritonavir	5	1	4
Tocilizumab	2	0	2
Remdesivir	1	0	1
Antiretroviral therapies			
TAF/FTC/bictegravir[a]	10	2	8
ABC/3TC/dolutegravir[a]	10	1	9
TAF/FTC + INI	6	1	5
Dolutegravir/3TC[a]	5	0	5
Dolutegravir + boosted PI	5	2	3
TAF/FTC + boosted PI	5	2	3
Other regimens	6	3	3

Abbreviations: ABC, abacavir; COVID-19, coronavirus disease 2019; FTC, emtricitabine; INI, integrase inhibitor; PI, protease inhibitor; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TAF, tenofovir, alafenamide; 3TC, lamivudine.

[a]Single-tablet regimen.

EARLY VIRUS CLEARANCE AND DELAYED ANTIBODY RESPONSE IN A CASE OF CORONAVIRUS DISEASE 2019 (COVID-19) WITH A HISTORY OF COINFECTION WITH HUMAN IMMUNODEFICIENCY VIRUS TYPE 1 AND HEPATITIS C VIRUS

Zhao J, Liao X, Wang H, Wei L, Xing M, Liu L, Zhang Z.. Clin Infect Dis. 2020 Nov 19;71(16):2233-2235. doi: 10.1093/cid/ciaa408.
Level of Evidence: Other - Case Report

BLUF

Hepatologists at the National Clinical Research Center for Infectious Disease in Shenzhen, China presented a 38-year-old male patient with HIV-1 and HCV who, despite testing negative for SARS-CoV-2 infection, had anti-SARS-CoV-2 antibodies and symptoms of infection. Authors propose this may be due to either anti-HIV agents having therapeutic effects against SARS-CoV-2 or high levels of type 1 IFN in HIV causing suppression of SARS-CoV-2. Results further showed delayed antibody response with IgM levels remaining elevated 42 days post-illness, and authors suggest coinfection with HIV-1 and HCV in COVID-19 patients may cause immune dysfunction leading to early clearance of and delayed antibody response to SARS-CoV-2.

SUMMARY

Further details of case report below:
A 38-year-old male with history of HIV-1 and HCV 4 was admitted to Shenzhen Third People's Hospital after presenting with fever (37.2°C) and muscle aches following travel to Wuhan, China. Chest CT showed pneumonia in the right lower lung, which resolved after treatment with oseltamivir and inhaled interferon-alpha. He was discharged 5 days later, after 3 negative SARS-CoV-2 swab tests. 42 days after onset of illness, plasma total antibody (Ab) was determined to be 13.2 cut off index (COI) and IgM specific for SARS-CoV-2 was 49.5 COI, indicating significantly lower plasma total Ab but higher IgM compared to other patients post-recovery from COVID-19. Seven days later plasma total Ab and IgM rose to 523.8 COI and 54 COI, respectively, detecting a delayed antibody response to SARS-CoV-2 infection.

ABSTRACT

The effect of host immune status on SARS-CoV-2 infection remains unknown. Here, we report the first case of COVID-19 with HIV-1 and HCV co-infection, who showed a persistently negative SARS-CoV-2 RNA test, but delayed antibody response in the plasma. This case highlights the influence of HIV-1-induced immune dysfunction on the early SARS-CoV-2 clearance.

UNDERSTANDING THE PATHOLOGY

EVIDENCE OF SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 REINFECTION AFTER RECOVERY FROM MILD CORONAVIRUS DISEASE 2019

Lee JS, Kim SY, Kim TS, Hong KH, Ryoo NH, Lee J, Park JH, Cho SI, Kim MJ, Kim YG, Kim B, Shin HS, Oh HS, Seo MS, Gwon TR, Kim Y, Park JS, Chin BS, Park WB, Park SS, Seong MW.. Clin Infect Dis. 2020 Nov 21:ciaa1421. doi: 10.1093/cid/ciaa1421. Online ahead of print.
Level of Evidence: 4 - Case-series or case-control studies, or poor quality prognostic cohort study

BLUF

Investigators, primarily from Seoul National University College of Medicine, analyzed samples from 6 COVID-19-positive patients at 3 tertiary hospitals in South Korea. Each of these patients had recovered with negative SARS-CoV-2 rRT-PCR results and then presented again with subsequent positive rRT-PCR results. One of the patients, a 21-year-old female with allergic rhinitis, recovered with resolution of symptoms, then presented 2 additional times (April 5th and 30th, 2020) with mild symptoms and subsequent positive testing (Figure 2, 3). A whole-genome sequencing from samples taken at her first and her third presentations found two distinct genomic clades between the viral RNA in the 2 samples, suggesting evolutions of the SARS-CoV-2 genome. Of note, whole-genome sequencing was only able to be performed on this patient. However, these findings suggest that SARS-CoV-2 infection may not confer immunity against subsequent reinfections of different strains, and precaution should continue to be taken even after recovery.

ABSTRACT

BACKGROUND: Positive results from real-time reverse-transcription polymerase chain reaction (rRT-PCR) in recovered patients raise concern that patients who recover from coronavirus disease 2019 (COVID-19) may be at risk of reinfection. Currently, however, evidence that supports reinfection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has not been reported. METHODS: We conducted whole-genome sequencing of the viral RNA from clinical specimens at the initial infection and at the positive retest from 6 patients who recovered from COVID-19 and retested positive for SARS-CoV-2 via rRT-PCR after recovery. A total of 13 viral RNAs from the patients' respiratory specimens were consecutively obtained, which enabled us to characterize the difference in viral genomes between initial infection and positive retest. RESULTS: At the time of the positive retest, we were able to acquire a complete genome sequence from patient 1, a 21-year-old previously healthy woman. In this patient, through the phylogenetic analysis, we confirmed that the viral RNA of positive retest was clustered into a subgroup distinct from that of the initial infection, suggesting that there was a reinfection of SARS-CoV-2 with a subtype that was different from that of the primary strain. The spike protein D614G substitution that defines the clade "G" emerged in reinfection, while mutations that characterize the clade "V" (ie, nsp6 L37F and ORF3a G251V) were present at initial infection. CONCLUSIONS: Reinfection with a genetically distinct SARS-CoV-2 strain may occur in an immunocompetent patient shortly after recovery from mild COVID-19. SARS-CoV-2 infection may not confer immunity against a different SARS-CoV-2 strain.

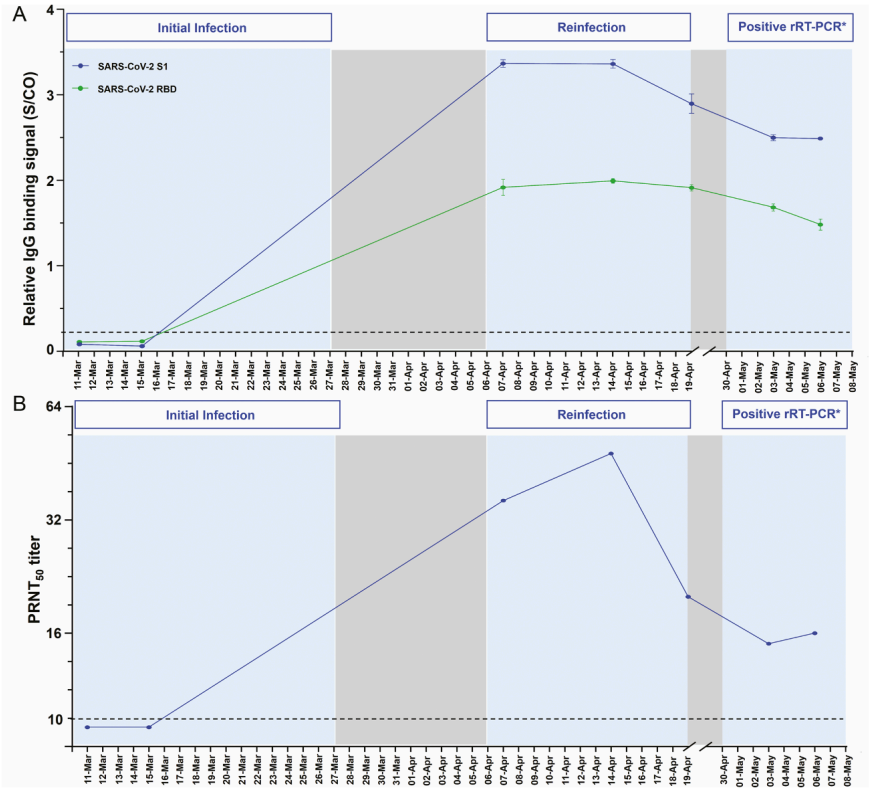

Figure 3. Temporal profile of antibodies in patient 1 with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) reinfection. Each antibody was measured at 7 time points. A, IgG antibodies against SARS-CoV-2 S1 (blue) and receptor binding domain (green) protein. The cutoff values for IgG antibody assay were S/CO = 1. B, PRNT titers of neutralizing antibody. A PRNT50 titer was defined as the highest serum dilution that results in a reduction of >50% of the control plaque count. A PRNT50 titer of ≥10 was considered protective. Abbreviations: IgG, immunoglobulin G; PRNT, plaque-reduction neutralization test; rRT-PCR, real-time reverse-transcription polymerase chain reaction; S/CO, signal to cutoff. *No intact viral genome was observed at third admission.

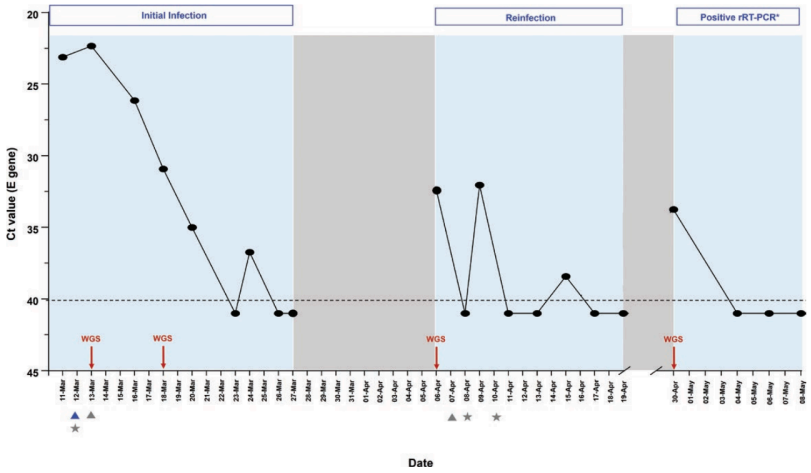

Figure 2. Temporal profile of the viral load in patient 1 with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) reinfection. WGS of SARS-CoV-2 from respiratory specimens was performed at 4 time points (at first admission with initial diagnosis, during follow-up, at second admission with reinfection, at third admission with retest positive again). A lower Ct value corresponds to a higher viral load. The values under the dashed line were interpreted as negative for SARS-CoV-2. Viral culture was conducted by inoculating upper (triangle) or lower (star) respiratory tract specimens onto Vero cells. Blue indicates that SARS-CoV-2 was culturable and gray indicates that SARS-CoV-2 was not culturable. *No intact viral genome was observed at third admission. Abbreviations: Ct, cycle threshold; rRT-PCR, real-time reverse-transcription polymerase chain reaction; WGS, whole-genome sequencing.

THE OPTIMAL DIAGNOSTIC METHODS FOR COVID-19

Harahwa TA, Lai Yau TH, Lim-Cooke MS, Al-Haddi S, Zeinah M, Harky A.. Diagnosis (Berl). 2020 Nov 18;7(4):349-356. doi: 10.1515/dx-2020-0058.
Level of Evidence: 5 - Review / Literature Review

BLUF

A team of British medical students and physicians conducted a literature review surrounding the various COVID-19 diagnostic methods. They conclude that RT-PCR is the most accurate method for diagnosing acute SARS-CoV-2 infection due to its high specificity/sensitivity and ability to provide rapid results. Based on their review, they claim current data indicates most other methodologies are limited. They recommend computed tomography only be used when imaging may affect management. Additionally, they found that ultrasound is limited by user ability and serologies are less accurate for diagnosing acute infection due to delayed antibody production (10 days for IgM and 20 days for IgG to be detectable after infection).

ABSTRACT

As the world continues to study and understand coronavirus disease (COVID-19), existing investigations and tests have been used to try and detect the virus to slow viral transmission and its global spread. A 'gold-standard' investigation has not yet been identified for detection and monitoring. Initially, computed tomography (CT) was the mainstay investigation as it shows the disease severity and recovery, and its images change at different stages of the disease. However, CT has been found to have limited sensitivity and negative predictive value in the early stages of the disease, and the value of its use has come under debate due to whether its images change the treatment plan, the risk of radiation, as well as its practicality with infection control. Therefore, there has been a shift to the use of other imaging modalities and tests, such as chest X-rays and ultrasound. Furthermore, the use of nucleic acid-based testing such as reverse-transcriptase polymerase chain reaction (RT-PCR) have proven useful with direct confirmation of COVID-19 infection. In this study, we aim to review and analyse current literature to compare RT-PCR, immunological biomarkers, chest radiographs, ultrasound and chest CT scanning as methods of diagnosing COVID-19.

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