American Journal of Epidemiology and Infectious Disease, 2021, Vol. 9, No. 1, 11-17
Available online at http://pubs.sciepub.com/ajeid/9/1/3
Published by Science and Education Publishing
DOI:10.12691/ajeid-9-1-3

Recurrent Symptomatic SARS-CoV-2 RT PCR Positivity among Healthcare Professionals: A Series of Cases

Kyle Martin S. Alimurung[1], Sigrid D. Santos[2], Maria Clarina D. Mariano[2], Aliza S. Concepcion[2], Janice C. Caoili[3,*]

[1]Department of Medicine, Makati Medical Center, #2 Amorsolo Street, Legazpi Village, Makati, 1229, Philippines
[2]Infection Prevention and Control Department, Makati Medical Center, #2 Amorsolo Street, Legazpi Village, Makati, 1229, Philippines
[3]Section of Infectious Disease, Department of Medicine, Makati Medical Center, #2 Amorsolo Street, Legazpi Village, Makati, 1229, Philippines
*Corresponding author: Janice.caoili@gmail.com

Received June 24, 2021; Revised July 27, 2021; Accepted August 06, 2021

Abstract Background: The ongoing COVID-19 pandemic has led to heightened health risk to health professionals from recurrent symptomatic SARS-CoV-2 infections due to continuous exposure in the workplace. Objectives: To highlight the need for universal clinical guidelines to provide clarity on appropriate interpretation and management of symptomatic recurrent positive SARS-CoV-2 reverse-transcription polymerase-chain-reaction (RT PCR) test results among healthcare professionals (HCPs) with a documented history of COVID-19 exposure. Methods: We present five cases of HCPs working at Makati Medical Center in the Philippines who previously recovered from symptomatic COVID-19 infection and presented at least 87 days after recovery with recurrent symptoms consistent with COVID-19 infection along with positive nasopharyngeal and oropharyngeal swab (NPS/OPS) RT PCR on repeat testing, suggesting recurrent infection. Results: Our cases had a disease-free average interval of 99 days (range of 87 to 124 days) between infection episodes. On serologic testing, only one case developed IgM and IgG antibodies after first infection. Four of five cases were deemed sources of infection transmission for new confirmed COVID-19 cases during at least one of their infection episodes. Discussion: Our cases highlight the dilemma of lack of universal clinical guidelines regarding appropriate interpretation of and management of recurrent positive SARS-CoV-2 RT PCR HCPs who are continuously exposed in clinical settings where limited or no access to genotyping and viral culture are available to validate reinfections, whether with prevalent strains and/or variants.

Keywords: *COVID-19, SARS-CoV-2 RT PCR, coronavirus, recurrent, serologic testing, healthcare professionals*

Cite This Article: Kyle Martin S. Alimurung, Sigrid D. Santos, Maria Clarina D. Mariano, Aliza S. Concepcion, and Janice C. Caoili, "Recurrent Symptomatic SARS-CoV-2 RT PCR Positivity among Healthcare Professionals: A Series of Cases." *American Journal of Epidemiology and Infectious Disease*, vol. 9, no. 1 (2021): 11-17. doi: 10.12691/ajeid-9-1-3.

1. Introduction

In December 2019, Chinese health authorities were alerted to an upsurge of pneumonia of unknown causes linked to a wholesale wet market in Wuhan, Hubei, China. [1,2,3,4] The etiology of the severe pneumonia has subsequently been identified as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), labelled COVID-19, which spread to 220 countries as of July 21, 2021. [5]

We present five cases of recurrent symptomatic SARS-CoV-2 RT PCR positive healthcare professionals (HCPs) working at our institution in whom symptoms had resolved, with negative results on RT PCR, and who experienced recurrent symptoms and retested positive on RT PCR at least 87 days later.

2. Methodology

Testing for SARS-CoV-2 through nasopharyngeal and oropharyngeal swab (NPS/OPS) RT PCR was performed for the following indications, namely: HCPs presenting with cough, fever, anosmia, colds or flu-like symptoms; were close contacts of a confirmed or suspected COVID-19 case; or during broad testing of staff from units with ongoing outbreak. All HCPs who tested positive were quarantined for at least 14 days and retested on or before day 14. Only HCPs with at least one negative NPS/OPS RT PCR test were cleared to return to work. Repeat testing was done for all HCPs who fulfilled the criteria for testing on more than one occasion. This workflow was in accordance with practices in place at our institution since February 2020, with NPS/OPS sampling

intended to improve the sensitivity and minimize false negatives. In all cases, RT PCR testing was performed using the Sansure Biotech Novel Coronavirus (2019-nCoV) Nucleic Acid Diagnostic Kit (PCR-Fluorescence Probing).

Contact tracing was conducted for HCPs who were suspected to have or were exposed to confirmed COVID-19 cases. High risk contacts were individuals who during the past 7 days, interacted with COVID-19 positive or suspected HCPs, within 2 meters for more than 15 minutes, and not wearing proper personal protective equipment. These individuals were advised to undergo swabbing.

Additionally, qualitative serologic testing for IgM and IgG to SARS-CoV-2 was performed on all HCPs from May 7 to June 1, 2020 using Innovita 2019-nCoV Ab Test (Colloidal Gold) for immunosurveillance.

2.1. Abbreviations and Acronyms

COVID-19 = coronavirus disease 2019
SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2
RT PCR = reverse-transcription polymerase-chain-reaction
2019-nCoV = Sansure Biotech Novel Coronavirus Nucleic Acid Diagnostic Kit
IgG = immunoglobulin G
IgM = immunoglobulin M
HCPs = healthcare professionals
CBC = complete blood count
RBC = red blood cell
WBC = white blood cell
MCH = mean corpuscular hemoglobin
CRP-HS = C-reactive protein high sensitivity
Trop I-HS = troponin I high sensitivity
Total CPK = total creatine phosphokinase
CPK MB= creatine phosphokinase myocardial band
LDH = lactate dehydrogenase
PaO2 = partial pressure of oxygen
iCa = ionized calcium
ECG = electrocardiogram
QTc = corrected QT interval
ED = emergency department
CT = cycle threshold
SD = standard deviation

3. Series of Five Cases

Five cases of HCPs with recurrent symptomatic SARS-CoV-2 RT PCR positivity were identified. Timelines and case information are summarized in Table 1 and Table 2, respectively, with case descriptions below.

Case 1

On March 28, 2020, a 28-year-old female delivery room nurse with bronchial asthma was exposed to two confirmed cases of COVID-19 infection. She self-quarantined at home on March 30.

On April 4, she developed a dry cough without other symptoms. Due to persistent coughing, she went to the emergency department (ED) on April 8 and was found positive for COVID-19 infection. She continued to self-isolate at home. Due to persistent cough, difficulty breathing, and anxiety, she was admitted to the COVID-19 dedicated floor on April 15. She had normal vital signs and an oxygen saturation of 99% on ambient air. Complete blood count (CBC) showed elevated hemoglobin, hematocrit, and red blood cell (RBC) count. Serum transaminases were elevated while electrolytes, D-dimer, procalcitonin, C-reactive protein high sensitivity (CRP-HS), troponin I high sensitivity (Trop I-HS), total creatine phosphokinase (total CPK), creatine phosphokinase MB (CPK MB), lactate dehydrogenase (LDH), ferritin, albumin, and renal function tests were within normal reference ranges. The 12-lead ECG showed normal sinus rhythm with prolonged QTc while a chest x-ray was normal. Repeat RT PCR tests were negative on April 15 and 18. She was discharged on April 19 and completed home isolation on April 23. Her symptoms completely resolved and she was allowed to return to work on April 24. On May 19, IgM and IgG were both negative.

On July 17, she was exposed to a confirmed COVID-19 case. On July 21, she experienced nasal congestion and tested positive by RT PCR. She underwent self-isolation for 14 days, during which her symptoms resolved. On August 5, a repeat RT PCR test was negative, and she was allowed to return to work on August 6, 2020.

On contact tracing, it was determined that she infected two close contacts (both confirmed by RT PCR) during her first COVID-19 infection episode but none during her second episode.

Case 2

On March 21, 2020, a 36-year-old dyslipidemic female delivery room nurse was exposed to a confirmed case of COVID-19. She underwent self-quarantine on March 28. On March 29, she developed a sore throat and dry cough. On March 30, due to persistent symptoms, she went to the ED where she tested positive for COVID-19. She was admitted to the COVID-19 dedicated floor. Her vital signs were normal, and oxygen saturation was 100% on ambient air. Procalcitonin and CRP-HS were elevated, while CBC, electrolytes, D-dimer, Trop I-HS, total CPK, LDH, ferritin, renal function, and liver function tests were within normal reference ranges. Antigen tests for influenza A and B were negative. Arterial blood gas analysis showed an arterial oxygen tension (PaO2) of 100 mmHg on ambient air. A 12-lead ECG showed normal sinus rhythm with prolonged QTc. Chest x-ray showed hazy opacities in the right lower lung (Figure 1A). RT PCR tests on April 2 and 4 were both positive. A repeat chest x-ray on April 5 showed minimal progression of hazy opacities in the right lower lung, and a new patch opacity in the left mid lung field (Figure 1B). She improved clinically and was discharged on April 6 to continue isolation at home, during which her symptoms eventually resolved. On April 30, a repeat RT PCR was negative, and she was allowed to return to work. Chest x-ray on May 2 showed significant clearing of opacities in the right lower lung and left mid lung fields (Figure 1C). On June 1, IgM and IgG were both positive.

On July 22, she experienced nasal congestion. Contact tracing revealed that she had again been exposed to a confirmed COVID-19 positive individual on July 20, two days prior to symptom onset. She self-isolated at home. She tested positive again by RT PCR on July 27. A chest

x-ray on July 27 was normal. She was confined at our institution for continued isolation from July 30 to August 8, during which she developed sore throat and odynophagia. On August 8, she tested negative and symptoms completely subsided by August 11. She was cleared to report for work on August 8, 2020.

On contact tracing, she was found not to have infected any close contacts during the first COVID-19 infection, but two close contacts during her second episode were found positive by RT PCR.

Table 1. Timeline of Cases

	Case 1	Case 2	Case 3	Case 4	Case 5
1st exposure	Day 0 (March 30)	Day 0 (March 21)	Day - indeterminate (due to continuous exposure in the ED)	Day 0 (March 25)	Day - indeterminate (due to return from vacation leave)
1st symptom	Day 7	Day 8	Day 0	Day 1	Day 0
+PCR	Day 11	Day 9, 12, 14	Day 0	Day 5	Day 2, 17
-PCR	Day 18, 21	Day 40	Day 10, 14	Day 27	Day 24
IgM, IgG	Day 52 (Neg, Neg)	Day 72 (Pos, Pos)	Day 52 (Neg, Neg)	Day 55 (Neg, Neg)	Day 30 (Neg, Neg)
2nd exposure	Day 111	Day 121	Day - indeterminate (due to continuous exposure in the ED)	Day 120	Day 109
2nd symptom	Day 115	Day 123	Day 134	Day 122	Day 111
+PCR	Day 115	Day 128	Day 134	Day 127	Day 111
-PCR	Day 130	Day 140	Day 147	Day 141	Day 121

Table 2. Summary of Case Information

Case	Age/role in the hospital/general health status	Time between 1st and 2nd episodes*	Clinical characteristics and radiologic imaging results	Timing of RT-PCR and Ct values	Number of Exposed Contacts who became positive by RT PCR	Antibody testing	Outcome
1	28/ Delivery room nurse/ Bronchial asthma	97 days	1st episode: dry cough, difficulty breathing, anxiety; normal chest x-ray 2nd episode: nasal congestion; no repeat chest x-ray	1st episode: positive four days post symptom onset (Ct values not available) 2nd episode: positive on first day of symptoms (N gene – 32.86, ORF gene – 35.45)	1st episode: two 2nd episode: zero	1st episode: IgM and IgG negative 45 days post symptom onset 2nd episode: no antibody testing performed	Fully recovered
2	36/ Delivery room nurse/ Dyslipidemia	88 days	1st episode: sore throat, dry cough; hazy opacities in the right lower lung on chest x-ray 2nd episode: nasal congestion and irritation; normal chest x-ray	1st episode: positive one day post symptom onset (Ct values not available) 2nd episode: positive five days post symptom onset (N gene – 34.02, ORF gene – 35.7)	1st episode: one 2nd episode: two	1st episode: IgM and IgG positive 64 days post symptom onset 2nd episode: no antibody testing performed	Fully recovered
3	27/ ED resident/ Essential thrombocythemia	124 days	1st episode: dry cough; normal chest x-ray 2nd episode: dry cough, nasal congestion; normal chest x-ray	1st episode: positive on first day of symptoms (Ct values not available) 2nd episode: positive on first day of symptoms (N gene – 28.57, ORF gene – 35.36)	1st episode: zero 2nd episode: one	1st episode: IgM and IgG negative 52 days post symptom onset 2nd episode: no antibody testing performed	Fully recovered
4	29/ Radiology nurse/ Migraines	100 days	1st episode: dizziness, fever, malaise, sore throat, nasal congestion; normal chest x-ray 2nd episode: nasal congestion, anosmia, sore throat; no repeat chest x-ray	1st episode: positive four days post symptom onset (Ct values not available) 2nd episode: positive five days post symptom onset (N gene – 34.48, ORF gene – 36.09)	1st episode: zero 2nd episode: two	1st episode: IgM and IgG negative 54 days post symptom onset 2nd episode: no antibody testing performed	Fully recovered
5	28/ Nursing aide/ immunocompetent	87 days	1st episode: fever, dry cough; chest x-ray not available 2nd episode: malaise, myalgia, easy fatigability, dyspnea on exertion; normal chest x-ray	1st episode: positive two days post symptom onset (N gene – undetermined, ORF gene – 39.82) 2nd episode: positive on first day of symptoms (N gene – 37.95, ORF gene – undetermined)	1st episode: zero 2nd episode: zero	1st episode: IgM and IgG negative 30 days post symptom onset 2nd episode: no antibody testing performed	Fully recovered

*1st negative after last positive RT PCR of 1st episode to 1st positive RT PCR of 2nd episode.

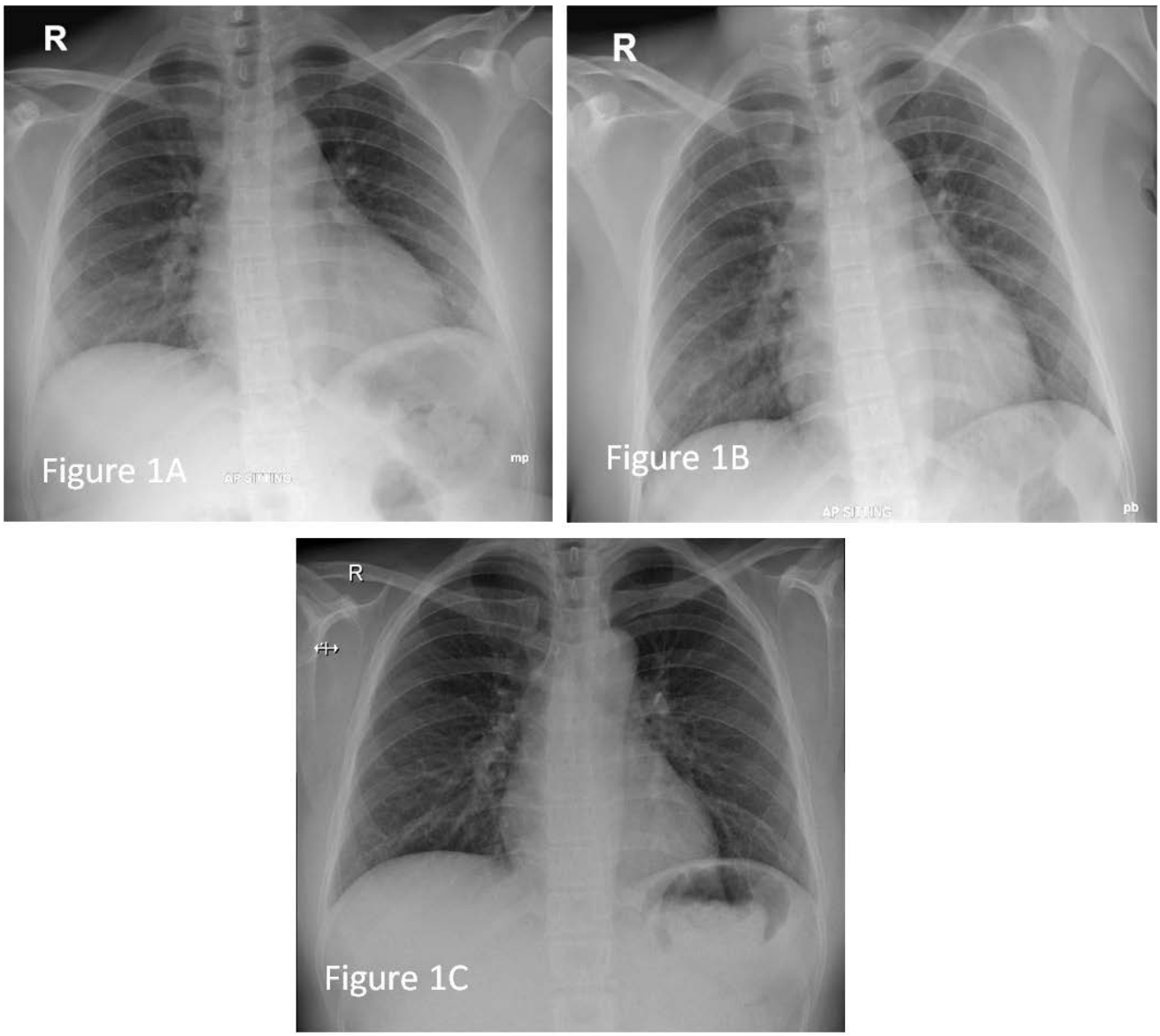

Figure 1. Chest x-ray images. (Figure 1A) March 30, 2020. (Figure 1B) April 5, 2020. (Figure 1C) May 2, 2020

Case 3

On March 16, 2020, a 27-year-old female ED resident, with essential thrombocythemia, presented at the ED with a dry cough. RT PCR was positive. She had normal vital signs, 99% oxygen saturation on ambient air, and negative antigen tests for influenza A and B. Laboratory examinations showed CBC with increased platelets and white blood cells (WBCs), with decreased mean corpuscular hemoglobin (MCH). CRP-HS, LDH, and ionized calcium (iCa) were increased while electrolytes, Trop I-HS, total CPK, CPK MB, ferritin, renal function, and liver function tests were normal. Chest x-ray was normal. She was sent home for 14-day self-isolation.

Repeat RT PCR swabs on March 26 and 30 done by the Makati City Health Department were negative, so she was allowed to return to work. On May 7, IgM and IgG were both negative.

On July 28, she again experienced a dry cough with nasal congestion and retested positive on RT PCR. Laboratory examinations showed CBC with increased RBC and platelets with decreased MCH. Chest x-ray was normal. She was again sent home for 14-day self-isolation. On August 10, 2020, RT PCR test was negative and symptoms had resolved. She was allowed to return to work after completing self-isolation.

On contact tracing, she was found not to have infected any close contacts during her first COVID-19 infection, but one close contact during her second episode subsequently tested positive by RT PCR.

Case 4

On March 25, 2020, a 29-year-old male radiology department nurse with a history of migraine was exposed to a confirmed COVID-19 case. He complained of dizziness, fever, malaise, sore throat, and nasal congestion on March 26 when he consulted at the ED. Since he had only mild symptoms, he was sent home for 14-day self-quarantine. On March 30, due to persistent symptoms, he returned to the ED, where he tested positive by RT PCR. His vital signs, CBC, and chest x-ray were normal. He was sent home to continue self-isolation. A repeat RT PCR test was negative on April 21, and he was allowed to return to work. On May 19, IgM and IgG were both negative.

On July 23, he was exposed to a suspected COVID-19 case. He developed nasal congestion and anosmia on July

25. On July 30, due to nasal congestion, anosmia, and sore throat, he consulted at the ED and retested positive by RT PCR. He was sent home for 14-day self-isolation during which his symptoms markedly improved, with minimal persistent nasal congestion. On August 13, 2020, he tested negative by RT PCR.

On contact tracing, he was found not to have infected any close contacts during the first COVID-19 infection. However, during his second episode, he was suspected to have infected two close contacts who both subsequently tested positive by RT PCR.

Case 5

On April 22, 2020, a 28-year-old female nursing aide, on the COVID-19 dedicated floor, complained of fever and dry cough. She was advised to go to the ED for RT PCR and tested positive on April 24. She was confined at our institution for isolation. Her repeat RT PCR tests on May 9 and 16 were positive and negative, respectively. On May 22, IgM and IgG were both negative. Her symptoms resolved during isolation and she was discharged on May 23. She was allowed to return to work the next day.

On August 9, she was exposed to several confirmed COVID-19 patients in the hospital. On August 11, she experienced generalized malaise, myalgia, easy fatigability, and dyspnea on exertion. She consulted at the hospital employee clinic where she tested positive by RT PCR. She was again confined at our institution. Her chest x-ray was normal. She experienced sore throat and odynophagia. On August 21, RT PCR testing was negative and she was discharged on August 25, 2020.

On contact tracing, she was found not to have infected any close contacts during both COVID-19 infection episodes.

4. Discussion

We present five cases of HCPs working at our institution, providing direct patient care, who were all previously diagnosed with symptomatic COVID-19. All cases had an initial RT PCR confirmed COVID-19 infection followed by convalescence, during which they each tested negative by RT PCR at least once. After recovery and return to work, they again developed symptoms after exposure to COVID-19 infected individuals and tested positive on repeat RT PCR. The shortest interval between consecutive COVID-19 diagnoses was 87 days (Table 2).

There are currently no universal clinical guidelines regarding appropriate interpretation of recurrent positive SARS-CoV-2 RT PCR results of symptomatic individuals. Several hypotheses have been proposed to explain this phenomenon. The two most frequently mentioned are discussed below in relation to our cases.

Firstly, several studies have found prolonged viral shedding among certain individuals infected with SARS-CoV-2, [6,7,8] while others suggest that the duration is variable. One study found that in mild infection, respiratory swabs may remain positive for two to 21 days, and even longer (five to 28 days) among asymptomatic. [9] Others have found that the duration of viral shedding has a median of 20 to 22 days [6,10,11,12] but can last up to 83 days. [8,13] Several reports indicate that patients who recover from COVID-19 may again test positive, [14] with a retest positivity rate at 14.5% [14,15] and 16.7% [14,16] during the 14-day isolation period of their first infection. [14] Gidari et al's case series and systematic review of presumptive recurrent cases showed that samples from six recurrent cases inoculated in culture on Vero E6 cells did not yield any replicable virus. [17] In their series, five cases tested positive for IgG to SARS-CoV-2. The authors concluded that their findings support the hypothesis that prolonged detection of SARS-CoV-2 from respiratory samples of recovered patients is due to viral remnants rather than recurrent infection. Since viral culture yielded negative results, they further concluded that these cases were most likely not infectious when they retested positive. This report also included a systematic review of 123 cases with recurrent positive swab results and found that the average number of days from first COVID-19 infection was 34.5 days (standard deviation, SD, 18.7 days). More than 70% of the cases were asymptomatic. In our series, the shortest duration from the recurrent positive swab result from the first COVID-19 infection was 87 days. All HCPs were symptomatic when they retested positive. From contact tracing of all HCPs who retested positive, we determined that four of the five HCPs had at least one contact who subsequently tested positive. Hence, the recurrent RT PCR positivity observed among our cases is difficult to explain on the basis of viral RNA remnants alone.

Secondly, there are a growing number of reports of suspected and confirmed cases of COVID-19 reinfection. The European Centre for Disease Prevention and Control summarized the first six cases of reinfection with laboratory confirmation using genomic sequencing. [18] The authors recommended utilizing epidemiologic, clinical, and virologic information to determine reinfection.

We suspect that the recurrent positive RT PCR results of our HCPs were infections rather than prolonged viral shedding in view of several factors. Importantly, the five HCPs were working in clinical areas, providing direct patient care, which put them at continuous risk for repeated exposure. Moreover, all of our cases were infected from March to early April 2020, when local community transmission of COVID-19 had just started, modes of viral transmission were not clearly defined, isolation protocols were not meticulously practiced, and community lockdowns had just begun. Our 5 HCPs experienced recurrent symptoms in July and August, when the country experienced a surge of infections after easing of community lockdowns in June. During their initial episode, all of the HCPs experienced symptoms consistent with COVID-19 infection and tested positive by RT PCR. They were cleared to return to work after they had completed at least 14 days of isolation, with symptom resolution and a negative RT PCR. The disease-free intervals averaged 99 days (range of 87 to 124 days). Furthermore, contact tracing revealed that four of the five HCPs were suspected sources of infection for other new confirmed cases.

Genotyping is unavailable at our institution for any of the five cases because samples from the initial COVID-19

infection were submitted to the national reference laboratory. Subsequent samples processed in our laboratory were also not stored. Because of the increasing cases of recurrent RT PCR positive HCPs at our hospital, we have started storing samples for sequencing. Our experience suggests that there may be more cases of recurrent positive SARS-CoV-2 RT PCR results which are not reported in literature because of local unavailability of genotyping.

We were unable to retrieve CT values of the samples taken during initial infection of our HCPs. Starting April 11, 2020, our molecular laboratory was accredited by the Philippine Department of Health to conduct RT PCR testing for SARS-CoV-2. The average cycle threshold (CT) values for the N gene and ORF gene for the second COVID-19 episodes of our cases were 34 and 36, respectively. Other investigators who have correlated RT PCR CT values and cultivable virus in cell culture found that samples with CT values above 30 did not yield culturable virus. [19] Moreover, other studies reported that their laboratories successfully cultured the virus only from specimens with CT values less than 25. [17] In our series, only case 3 had a CT value less than 30. However, since contact tracing revealed that four out of our five HCPs had a naive close contact who subsequently tested positive for COVID-19 infection, we cannot entirely rule out the possibility that the HCPs may have been contagious at the time they retested positive even if their CT values were greater than 30.

All five HCPs underwent IgM and IgG testing after the first episode, but only one HCP (case 2), who had documented pneumonia on chest x-ray had positive results (IgM and IgG). On average, the HCPs had serologic testing 49 days (range of 30 to 64 days) from onset of symptoms of the first episode. There is now a growing concern regarding SARS-CoV-2 reinfection particularly in light of a growing number of studies showing that antibody titers to SARS-CoV-2 may wane. [20] It is still unclear whether individuals with prior infections who test positive for antibodies to SARS-CoV-2 are completely or partially immune to reinfection.

We anticipate that there will be more cases of recurrent symptomatic SARS-CoV-2 positive cases among HCPs. Thus, it is imperative to develop case definitions for reinfection. Although genomic sequencing provides the ability to determine the infecting strains and/or variants, viral culture remains the only method to determine whether SARS-CoV-2 virus is culturable from repeat positive specimens. These technologies are not readily available in most health care institutions worldwide. Case definitions can provide guidance for health care providers in the management of HCPs with recurrent symptomatic positive SARS-CoV-2 RT PCR and determine appropriate management interventions, isolation, and contact tracing for HCPs with recurrent symptomatic positive results.

Our findings also underscore the crucial role of infection control in interrupting the chain of infection transmission in the hospital, considering that antibody mediated immunity produced after COVID-19 may wane and be insufficient to prevent repeated infection. We recognize that our case series has inherent limitations due to its observational design.

5. Conclusion

HCPs face the risk of repeated infection without the benefit of durable immunity from previous infection. Although it has been over a year since the onset of the pandemic, there remains an important gap of a need to develop universal clinical guidelines regarding appropriate interpretation of recurrent positive SARS-CoV-2 RT PCR results among HCPs with a documented history of COVID-19 infection. The guidelines should take into consideration that diagnostic tests such as genotyping and viral culture are not readily available in most healthcare institutions worldwide. Importantly, guidelines should provide practical guidance, including class of recommendation and strength of evidence for rational decision-making, as to the need for treatment, isolation, and contact tracing.

Acknowledgements

Role of the funding source: no funding

Declarations of Interest: the authors have no competing interests

The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

This case series was given approval by the Makati Medical Center Institutional Review Board on August 25, 2020.

We would like to thank Makati Medical Center Molecular and Immunology Laboratories for providing test results and other information related to COVID-19 testing procedures. We would also like to thank Salvador Eugenio Caoili, MD and Benjamin N. Alimurung, MD for reviewing the manuscript and providing valuable feedback.

References

[1] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. *Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China*. The Lancet. 2020; 395(10223): 497-506.

[2] Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. *Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia*. New England Journal of Medicine. 2020; 382(13): 1199-207.

[3] Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. *A Novel Coronavirus from Patients with Pneumonia in China, 2019*. New England Journal of Medicine. 2020; 382(8): 727-33.

[4] Adhikari SP, Meng S, Wu Y-J, Mao Y-P, Ye R-X, Wang Q-Z, et al. *Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of coronavirus disease (COVID-19) during the early outbreak period: a scoping review*. Infectious Diseases of Poverty. 2020; 9(1).

[5] University JH. *COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU)*. 2021.

[6] Duggan NM, Ludy SM, Shannon BC, Reisner AT, Wilcox SR. *A case report of possible novel coronavirus 2019 reinfection*. The American Journal of Emergency Medicine. 2020.

[7] Chen D, Xu W, Lei Z, Huang Z, Liu J, Gao Z, et al. *Recurrence of positive SARS-CoV-2 RNA in COVID-19: A case report*. International Journal of Infectious Diseases. 2020; 93: 297-9.

[8] Hoang VT, Dao TL, Gautret P. *Recurrence of positive SARS-CoV-2 in patients recovered from COVID-19*. Journal of Medical Virology. 2020.

[9] Yongchen Z, Shen H, Wang X, Shi X, Li Y, Yan J, et al. *Different longitudinal patterns of nucleic acid and serology testing results based on disease severity of COVID-19 patients.* Emerging Microbes & Infections. 2020; 9(1): 833-6.

[10] Lan L, Xu D, Ye G, Xia C, Wang S, Li Y, et al. *Positive RT-PCR Test Results in Patients Recovered From COVID-19*. JAMA. 2020; 323(15):1502.

[11] Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. *Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study*. The Lancet. 2020; 395(10229): 1054-62.

[12] Xiao AT, Tong YX, Gao C, Zhu L, Zhang YJ, Zhang S. *Dynamic profile of RT-PCR findings from 301 COVID-19 patients in Wuhan, China: A descriptive study*. Journal of Clinical Virology. 2020; 127: 104346.

[13] Li N, Wang X, Lv T. *Prolonged SARS-CoV-2 RNA shedding: Not a rare phenomenon*. Journal of Medical Virology. 2020.

[14] Kang H, Wang Y, Tong Z, Liu X. *Retest positive for SARS-CoV-2 RNA of "recovered" patients with COVID-19: Persistence, sampling issues, or re-infection?* Journal of Medical Virology. 2020.

[15] An J, Liao X, Xiao T, Qian S, Yuan J, Ye H, et al. Clinical characteristics of the recovered COVID-19 patients with re-detectable positive RNA test. 2020.

[16] Huang J, Zheng L, Li Z, Hao S, Ye F, Chen J, et al. Recurrence of SARS-CoV-2 PCR positivity in COVID-19 patients: a single center experience and potential implications. 2020.

[17] Gidari A, Nofri M, Saccarelli L, Bastianelli S, Sabbatini S, Bozza S, et al. *Is recurrence possible in coronavirus disease 2019 (COVID-19)? Case series and systematic review of literature*. European Journal of Clinical Microbiology & Infectious Diseases. 2020.

[18] European Centre for Disease Prevention and Control. *Reinfection with SARS-CoV-2: considerations for public health response*. 2020.

[19] Rhee C, Kanjilal S, Baker M, Klompas M. *Duration of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infectivity: When Is It Safe to Discontinue Isolation?* Clinical Infectious Diseases. 2020.

[20] Christensen J. British study shows evidence of waning immunity to Covid-19 2020 [updated October 27, 2020. Available from: https://edition.cnn.com/2020/10/26/health/covid-19-immunity-wanes-large-study-finds/index.html.