Detection of SARS-CoV-2 in peritoneal fluid from patients with kidney disease and COVID-19: report of two cases

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Case Report

Keywords: COVID-19, SARS-CoV-2, peritoneal fluid, peritoneal dialysis

Posted Date: September 16th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-79032/v1

Abstract

Background: Coronavirus disease-2019 (COVID-19) has a broad clinical presentation, involving multiple organs besides the respiratory system. Currently, there is little evidence available on the presence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in peritoneal fluid (PF). In this study, we describe the detection of SARS-CoV-2 in the PF of two patients with COVID 19 and kidney disease.

Case presentation: Case 1: A 71-year-old woman with a history of end-stage kidney disease who presented with a 15-day evolution of progressive dyspnea, accompanied by dry cough and fever; IgM antibodies to SARS-CoV-2 were detected on admission. Real-time SARS-CoV-2 polymerase chain reaction (qRT-PCR) in the PF was positive. Three days after admission the patient's respiratory distress improved and she was discharged after 8 days of hospitalization.

Case 2: A 78-year-old woman, with type 2 diabetes, hypertension, a 15-day history of polypnea, and a 5-day onset of fever and dyspnea. IgM and IgG antibodies to SARS-CoV-2 were detected on admission, as well as a positive nasopharyngeal qRT-PCR test for SARS-CoV-2. During hospitalization she developed acute kidney injury, requiring peritoneal dialysis, SARS-CoV-2 was confirmed in PF by qRT-PCR

Conclusions: These two cases highlights the importance of increasing the level of awareness for the presence and possible SARS-CoV-2 transmission through non-respiratory routes, like peritoneal fluid.

Emphasis should be given to appropriate preventive strategies for minimizing the risk of transmission of COVID-19 from patients on peritoneal dialysis in both inpatient and outpatient settings.

Background

On December 31st, 2019, the World Health Organization (WHO) notified about a series of 27 patients with pneumonia of unknown etiology in the city of Wuhan, China. Seven days after, a new type of coronavirus was described and later called Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Afterwards, it emerged as a global pandemic, affecting > 200 countries worldwide (1).

Coronavirus disease-2019 (COVID-19) predominantly affects the respiratory system, and the majority of the cases are mild. However, 14% are severe cases, while 5% of the cases develop acute respiratory distress syndrome or critical illness (2). Acute Kidney Injury (AKI) occurs in almost 17% of patients (3). Peritoneal dialysis (PD) has been proved as an efficient renal replacement therapy (RRT) in AKI (4). Since health care systems have been overwhelmed by the pandemic, and many COVID-19 centers do not have enough personal nor resources to offer intermittent hemodialysis (IH) or continuous extracorporeal renal replacement therapy (CRRT) to all patients, the use of acute PD has been proposed as an appropriate option for COVID-19 patients with AKI (5).

Acute PD with a flexible PD catheter has similar mortality and kidney function recovery outcomes when compared with CRRT in critically ill patients with AKI (6). Moreover, acute PD offers other advantages in

the treatment of AKI in COVID-19, as it requires minimal staff training, minimizing exposure to contagious patients; involves less use of personal protective equipment (PPE), is not affected by hypercoagulability, does not requires a vascular access, and offers more hemodynamic stability than IH (5). Furthermore, one advantage is that percutaneous catheter insertion does not require general anesthesia; therefore, it compromised less the respiratory function (4).

SARS-CoV-2 spreads primarily through respiratory secretions droplets, either directly or by contamination of hands and surfaces, in addition to aerosol secretions (7). Other human secretions have been identified as potential ways of transmission, such as feces, blood, conjunctival, and tears (8–10). It is not uncommon that health care workers have to deal with peritoneal fluid (PF), which follows a particular disposal procedure. To our knowledge, until now, it has not been described whether PD can contribute to the spread of the virus (viral cultures of this fluid have not been performed); furthermore, it is unknown if there is an expression of angiotensin-converting enzyme 2 (ACE2) in peritoneum cells (11).

Currently, the presence of SARS-CoV-2 in PF remains controversial. Some reports have identified the presence of genetic material in the PF, and it was associated with PD failure (12,13). However, other reports have not detected the presence of the virus in the PF (14–17).

In this paper, we present two patients with kidney disease who required RRT with PD in whom the presence of viral ribonucleic acid (RNA) was detected in the PF.

In all samples, SARS-CoV-2 detection was performed under the same conditions. Briefly, viral RNA was extracted using the QIAamp Viral RNA Mini Kit (Qiagen, Hilden, Germany) in a BSL2 facility. RNA was assessed by quantitative Reverse Transcription-Polymerase Chain Reaction (qRT-PCR) using the Berlin protocol's primer design and thermal cycling conditions (55°C for 10 min for reverse transcription, followed by 95°C for 3 min and then 45 cycles of 95°C for 15 s, 58°C for 30 s). The WoV19 kit (Genes2life, Guanajuato, Mexico) was used for the detection of SARS-CoV-2. qRT-PCR determinations were performed in a CFX-96 thermocycler (Bio-Rad, California, USA). Furthermore, Cellex's (North Carolina, USA) lateral flow immunoassay was used for the determination of SARS-CoV-2 IgG/IgM as a rapid test.

Case Presentation

Case 1

A 71-year-old woman with end-stage kidney disease (ESKD) on CAPD, type 2 diabetes, hypertension, and neurogenic bladder, was admitted to the COVID-19 unit, with a two-week history of shortness of breath, dry cough, and a one-day onset of fever. On admission, she had a low oxygen saturation (88%), she was normotensive, with a respiratory rate of 24 breaths per minute, a heart rate of 89 beats per minute, and a body temperature of 37ºC. A chest X-ray showed diffuse opacities and consolidation in the base of the right lung. A COVID-19 rapid test of IgG/IgM was positive for IgM; a nasopharyngeal qRT-PCR test for SARS-CoV-2 was negative. Two days after admission, she presented PD catheter dysfunction. Additionally, a bacterial pneumonia infection was also suspected both by the patient's clinical findings

and laboratory tests (Table 1). Empirical piperacillin/tazobactam was initiated. Subsequently, she required ventilatory support with supplementary oxygen. A qRT-PCR test for SARS-CoV-2 was performed in the PF that had remained for 48 hours in the peritoneal cavity. The molecular test was positive. [cycle threshold (Ct)=36 and Ct=22 for E, and RNase P genes, respectively]. The RdRP gene did not amplify. RP was used as an endogenous internal amplification control. A time-dependent follow-up of SARS-CoV-2 presence in the PF was performed, and samples of PF that remained in the peritoneal cavity at different periods of time (4, 12, and 24 hours), were analyzed (Table 3).

Three days after hospitalization, the patient's respiratory distress improved, and her PD catheter was working well. A PF culture detected methicillin-sensitive *Staphylococcus aureus*. She was discharged after 8 days of hospitalization, with antibiotic and isolation indications. Fourteen days after her discharge, her PF culture, leucocyte cells count, and qRT-PCR test for SARS-CoV-2 were negative.

Table 1. Laboratory test during hospital admission and discharge

	Admission	Discharge
Hb g/dL	8.0	8.6
Ls $x10^3/mm^3$	9.5	9.06
Lymph %	18.4	21.8
Plt $x10^3/mm^3$	486.5	500
LDH U/L	-	240
CRP mg/L	98.0	30.8
sFer ng/mL	115.0	100.9
PCT ng/mL	1.2	0.4
LsPF $x10^3/mm^3$	15.8	66
PMNPF %	89	91
sCr mg/dL	3.3	3.5
sUr mg/dL	28.9	40.2

Hb, hemoglobin; Ls, leucocytes; Lymph, lymphocytes; Plt, platelets; LDH, lactic dehydrogenase; CRP, C-reactive protein; sFer, serum ferritin; PCT, procalcitonin; LsPF, leucocytes in peritoneal fluid; PMNPF,

polymorphonuclear cells in peritoneal fluid; sCr, serum creatinine; sUr, Serum urea.

Case 2:

A 78-years-old woman with type 2 diabetes, hypertension, chronic obstructive pulmonary disease, and ischemic heart disease, arrived at the COVID-19 unit, referring a two-week history of polypnea; five days before admission, she developed fever, nausea, myalgias, cough, and shortness of breath. Oxygen saturation upon admission was <86%; blood pressure was 205/116 mm/Hg. Bilateral lung crackling without whistling was detected. Her chest X-ray showed global cardiomegaly, with increased density in both upper lung zones, perihilar opacities, and bilateral air bronchograms. A COVID-19 rapid test of IgG/IgM was positive for both IgG and IgM, as well as a positive nasopharyngeal qRT-PCR test for SARS-CoV-2.

Laboratory tests showed glomerular filtration rate (GFR) of 48 mL/min/1.73m^2 estimated with the (CKD-EPI) formula (18), decompensated diabetes, and thrombocytopenia; five days after admission, she developed KDIGO III AKI and uremic encephalopathy (Table 2). A percutaneous tenckhoff catheter was placed at the bedside, and automated cycler PD was started. A PF sample obtained during the catheter placement was positive to qRT-PCR SARS-CoV-2 test (Ct=34, Ct=41, Ct=32 for E, RdRP, and RNase P genes, respectively). Although the presence of SARS-CoV-2 was confirmed in PF (Table 3), the patient never had peritoneal or gastrointestinal symptoms. Fortunately, the patient's kidney function improved, and the catheter was removed on day 12 and discharged the day after.

The PFs of both patients were disposed by infusing chlorinated solution (Amukina ® at 50%) through the tubes and bags (19). Then, the liquid was disposed to a chlorinated septic tank.

Table 2. Laboratory test during hospital admission, PD start day and discharge.

	Admission	PD start	Discharge
Hb g/dL	13	15	10
Ls x10^3/mm^3	11.26	11.34	16.47
Lymph %	20.1	6.7	11.0
Plt x10^3/mm^3	79.6	282	185
LDH U/L	177	-	112
CRP mg/L	17.4	-	14.8
sFer ng/mL	75.5	-	239.4
PCT ng/mL	12.5	1.16	0.09
sCr mg/dL	1.1	2.5	0.57
sUr mg/dL	65	317	84

Hb, hemoglobin; Ls, leucocytes; Lymph, lymphocytes; Plt, platelets; LDH, lactic dehydrogenase; CRP, C-reactive protein; sFer, serum ferritin; PCT, procalcitonin; sCr, serum creatinine; sUr, Serum urea; PD, peritoneal dialysis.

Table 3. Nasopharyngeal and Peritoneal Fluid SARS-CoV-2 PCR

Patient	qRT-PCR NFEx	qRT-PCR PF	Hours in cavity	IgG Ab	IgM Ab
Case 1	-	+	48: + 4: - 12: - 24: -	-	+
Case 2	+	+	+	+	+

qRT-PCR, quantitative Reverse Transcription-Polymerase Chain Reaction; NFEx, nasopharyngeal exudate; PF, peritoneal fluid; IgG, immunoglobulin G; IgM, immunoglobulin M; Ab, antibody, SARS CoV-2, severe

acute respiratory syndrome coronavirus 2.

Discussion And Conclusions

These two case reports alert about the presence of a high viral load of SARS-CoV-2 in PF, which could potentially be a way of transmission to health personnel, as well as to the community.

There are reports on the detection by qRT-PCR test of SARS-CoV-2 in different types of human specimens, such as bronchoalveolar, sputum, nasal and pharyngeal fluids, feces, blood, urine, and, most recently, PF. The viral loads are different between these specimens, being higher in bronchioalveolar secretions (8,13,17). We present two cases of patients on PD with COVID-19 in whom the presence of viral RNA was found in the PF. The first case, a patient on CAPD, who developed bacterial peritonitis due to methicillin-sensitive *S. aureus*, and respiratory symptoms compatible with COVID-19 with a rapid test positive for IgM, and negative nasopharyngeal qRT-PCR test for SARS-CoV-2 (Table 3). The fifteen-day evolution of symptoms in this patient could explain the negative qRT-PCR. Nonetheless, the PF molecular analysis became positive at day 17 after symptoms onset (Figure 1); Although the reports of viral presence in PF are controversial, we carried out determinations at different times, being positive in the PF that remained in the cavity for 48 hours; we consider that this may be one of the explanations for the controversial reports of SARS-CoV-2 presence in PF. Thus, it is important to verify and expand the criteria for the determination of viral particles in time depending fashion of the duration of PD. Although the presence of the SARS-CoV-2 virus was detected in PF, it is essential to clarify that, since the viral load presented in the PF was above a Ct=34, this fluid had no infectious potential as reported by *La Scola et. al* (20).

The second case, diagnosed by a positive rapid test of IgG/IgM, plus a positive nasopharyngeal qRT-PCR test for SARS-CoV-2 (Table 3) required automated cycler PD due to AKI secondary to cardiovascular failure at day 5 of hospitalization (Figure 2). SARS-CoV-2 presence in PF was positive in the sample obtained during catheter placement. Importantly, the PF's viral load in this patient falls within the parameters of a viral load that has been determined to have an infective potential (20). For this reason, we emphasize the importance of searching SARS-CoV-2 in PF based on the patient’s characteristics and COVID-19 infection evolution.

Both cases tested positive to viral genetic material to SARS-CoV-2 in PF. A possible explanation for this is the immunosuppressed state that exists during a uremic state caused by: a) decreased phagocytic function of granulocytes, as well as monocytes/ macrophages (21–23); b) dysfunction of antigen presentation capacity, through the depletion of dendritic cells, the primary antigen-presenting cells (23–25); c) low capacity of B lymphocytes to produce antibodies, resulting in a reduced number of antibodies, altering the humoral immune response (23,26–28); and d) impaired cell-mediated immunity, due to increased T cell turnover and apoptosis, leading to depletion of *naïve* and central memory $CD4^+$ T-cells, as well as $CD8^+$ T-cells (23,27,29–31).

A better understanding of how this virus is transmitted is key to stopping its spread. Thus, knowing whether PF could be a form of transmission is crucial. Nowadays, it is urgent to achieve viral isolation in cultures to identify an infective potential, so until then, appropriate preventive strategies must, therefore, be rapidly employed to minimize the risk of COVID-19 among patients on peritoneal dialysis in outpatient facilities (32).

ACE2 is expressed in the gastrointestinal tract and could be injured directly via entry into enterocytes or indirectly via the host inflammatory response (16,33), but not all publications have demonstrated the virus presence in PF. In our CAPD patient, bacterial peritonitis was present when the sample was taken, while in the AKI patient, the severity of the infection and kidney and heart stress were evident. Some explanation for this could be the upregulated inflammatory response in peritoneum through some ACE2 polymorphisms which have been detected in animal models linked to cardiovascular disease (33).

In conclusion, we present two cases of patients on PD with COVID-19 in whom the presence of viral RNA was confirmed in the PF. Since PD is frequently used in patients with COVID-19 and AKI as well as in ESKD patients in low-resource settings like ours, the proper handling and disposal of PF is essential.

Uremic syndrome causes an immunosuppressive state that could favor a high viremia in the PF. It is unknown whether the genetic material detected through the qRT-PCR test in PF can be infectious; it is imperative to provide a correct training in fluid handling, for both health personnel, as well as patients and their families, and future studies about this topic are necessary.

Finally, with current information, it may be necessary to recommend the use of PPE to health personnel and families of patients on PD, especially during the early stages of the disease, where the viral load may be increased, and the PF is considered potentially infectious. This recommendation should be followed regardless of the absence of symptoms compatible with COVID-19. Unique protocols for the appropriate handling, inactivation, and disposal of PF should be implemented to reduce the risk of viral transmission that could occur in this way.

Declarations

Ethics approval and consent to participate

Both patients signed written informed consent for the clinical care. Our study has been granted an exemption from review by the ethics committee in research of the “Antiguo Hospital Civil de Guadalajara – Fray Antonio Alcalde."

Consent for publication

Written informed consent for publication of their clinical details and clinical images was obtained from both patients. Furthermore, both case reports have not been published in any other paper.

Availability of data and materials

All the data supporting our findings is contained within the manuscript.

Competing interests

The authors declare that they have no competing interests

Funding

No funding was obtained for this study

Authors' contributions

I-HM, A-VML, A-DSA, and G-SR treated the patients and took the samples. S-RK, C-SRI, A-ZM, and A-JJC performed the test. R-HVV, A-VJF, G-GG, and G-HLA analyzed the cases, I-HM, A-VML, R-HVV, and G-HLA wrote the manuscript. A-VJF, G-GG, S-RK, C-SRI, A-ZM, and A-JJC corrected the manuscript. All authors have read and approved the manuscript.

Acknowledgements

Not applicable

Abbreviations

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

COVID-19: coronavirus disease-2019

qRT-PCR: quantitative Reverse Transcription-Polymerase Chain Reaction

IgM: Immunoglobulin M

IgG: Immunoglobulin G

PF: peritoneal fluid

WHO: world health organization

AKI: acute kidney injury

PD: peritoneal dialysis

RRT: renal replacement therapy

IH: hemodialysis

CRRT: continuous extracorporeal renal replacement therapy

PPE: personal protective equipment

ACE2: angiotensin-converting enzyme 2

CAPD: continuous peritoneal ambulatory dialysis

RNA: ribonucleic acid

ESKD: end-stage kidney disease

Ct: cycle threshold

GFR: glomerular filtration rate

CKD-EPI: chronic kidney disease epidemiology collaboration

KDIGO: kidney disease improving global outcomes

References

1. World Health Organization. WHO Coronavirus Disease (COVID-19) Dashboard.
2. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China. JAMA [Internet]. 2020 Apr 7;323(13):1239. Available from: https://jamanetwork.com/journals/jama/fullarticle/2762130
3. Robbins-Juarez SY, Qian L, King KL, Stevens JS, Husain SA, Radhakrishnan J, et al. Outcomes for Patients With COVID-19 and Acute Kidney Injury: A Systematic Review and Meta-Analysis. Kidney Int Reports [Internet]. 2020 Aug;5(8):1149–60. Available from: https://linkinghub.elsevier.com/retrieve/pii/S246802492031336X
4. Vigiola Cruz M, Bellorin O, Srivatana V, Afaneh C. Safety and Efficacy of Bedside Peritoneal Dialysis Catheter Placement in the COVID-19 Era: Initial Experience at a New York City Hospital. World J Surg [Internet]. 2020 Aug 26;44(8):2464–70. Available from: http://link.springer.com/10.1007/s00268-020-05600-4
5. Parapiboon W, Ponce D, Cullis B. Acute peritoneal dialysis in COVID-19. Perit Dial Int J Int Soc Perit Dial [Internet]. 2020 Jul 19;40(4):359–62. Available from: http://journals.sagepub.com/doi/10.1177/0896860820931235
6. Liu L, Zhang L, Liu GJ, Fu P. Peritoneal dialysis for acute kidney injury. Cochrane Database Syst Rev [Internet]. 2017 Dec 4; Available from: http://doi.wiley.com/10.1002/14651858.CD011457.pub2
7. Jin Y, Yang H, Ji W, Wu W, Chen S, Zhang W, et al. Virology, Epidemiology, Pathogenesis, and Control of COVID-19. Viruses [Internet]. 2020 Mar 27;12(4):372. Available from: https://www.mdpi.com/1999-4915/12/4/372
8. Wang W, Xu Y, Gao R, Lu R, Han K, Wu G, et al. Detection of SARS-CoV-2 in Different Types of Clinical Specimens. JAMA [Internet]. 2020 Mar 11; Available from:

https://jamanetwork.com/journals/jama/fullarticle/2762997

9. Colavita F, Lapa D, Carletti F, Lalle E, Bordi L, Marsella P, et al. SARS-CoV-2 Isolation From Ocular Secretions of a Patient With COVID-19 in Italy With Prolonged Viral RNA Detection. Ann Intern Med [Internet]. 2020 Aug 4;173(3):242–3. Available from: https://www.acpjournals.org/doi/10.7326/M20-1176
10. Xia J, Tong J, Liu M, Shen Y, Guo D. Evaluation of coronavirus in tears and conjunctival secretions of patients with SARS-CoV-2 infection. J Med Virol [Internet]. 2020 Jun 12;92(6):589–94. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.25725
11. Zou X, Chen K, Zou J, Han P, Hao J, Han Z. Single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection. Front Med [Internet]. 2020 Apr 12;14(2):185–92. Available from: http://link.springer.com/10.1007/s11684-020-0754-0
12. Vischini G, D'Alonzo S, Grandaliano G, D'Ascenzo FM. SARS-CoV-2 in the peritoneal waste in a patient treated with peritoneal dialysis. Kidney Int [Internet]. 2020 Jul;98(1):237–8. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0085253820305317
13. Coccolini F, Tartaglia D, Puglisi A, Giordano C, Pistello M, Lodato M, et al. SARS-CoV-2 Is Present in Peritoneal Fluid in COVID-19 Patients. Ann Surg [Internet]. 2020 Sep;272(3):e240–2. Available from: https://journals.lww.com/10.1097/SLA.0000000000004030
14. El Shamy O, Vassalotti JA, Sharma S, Aydillo-Gomez T, Marjanovic N, Ramos I, et al. Coronavirus disease 2019 (COVID-19) hospitalized patients with acute kidney injury treated with acute peritoneal dialysis do not have infectious peritoneal dialysis effluent. Kidney Int [Internet]. 2020 Sep;98(3):782. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0085253820307092
15. Ngaserin SH-N, Koh FH, Ong B-C, Chew M-H. COVID-19 not detected in peritoneal fluid: a case of laparoscopic appendicectomy for acute appendicitis in a COVID-19-infected patient. Langenbeck's Arch Surg [Internet]. 2020 May 9;405(3):353–5. Available from: http://link.springer.com/10.1007/s00423-020-01891-2
16. Seeliger B, Philouze G, Benotmane I, Mutter D, Pessaux P. Is the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) present intraperitoneally in patients with coronavirus disease 2019 (COVID-19) infection undergoing emergency operations? Surgery [Internet]. 2020 Aug;168(2):220–1. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0039606020303329
17. Candellier A, Goffin É. Letter regarding "SARS-CoV-2 in the peritoneal waste in a patient treated with peritoneal dialysis." Kidney Int [Internet]. 2020 Aug;98(2):512. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0085253820306608
18. Levey AS, Stevens LA, Schmid CH, Zhang Y (Lucy), Castro AF, Feldman HI, et al. A New Equation to Estimate Glomerular Filtration Rate. Ann Intern Med [Internet]. 2009 May 5;150(9):604. Available from: http://annals.org/article.aspx?doi=10.7326/0003-4819-150-9-200905050-00006
19. Kampf G, Todt D, Pfaender S, Steinmann E. Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents. J Hosp Infect [Internet]. 2020 Mar;104(3):246–51. Available

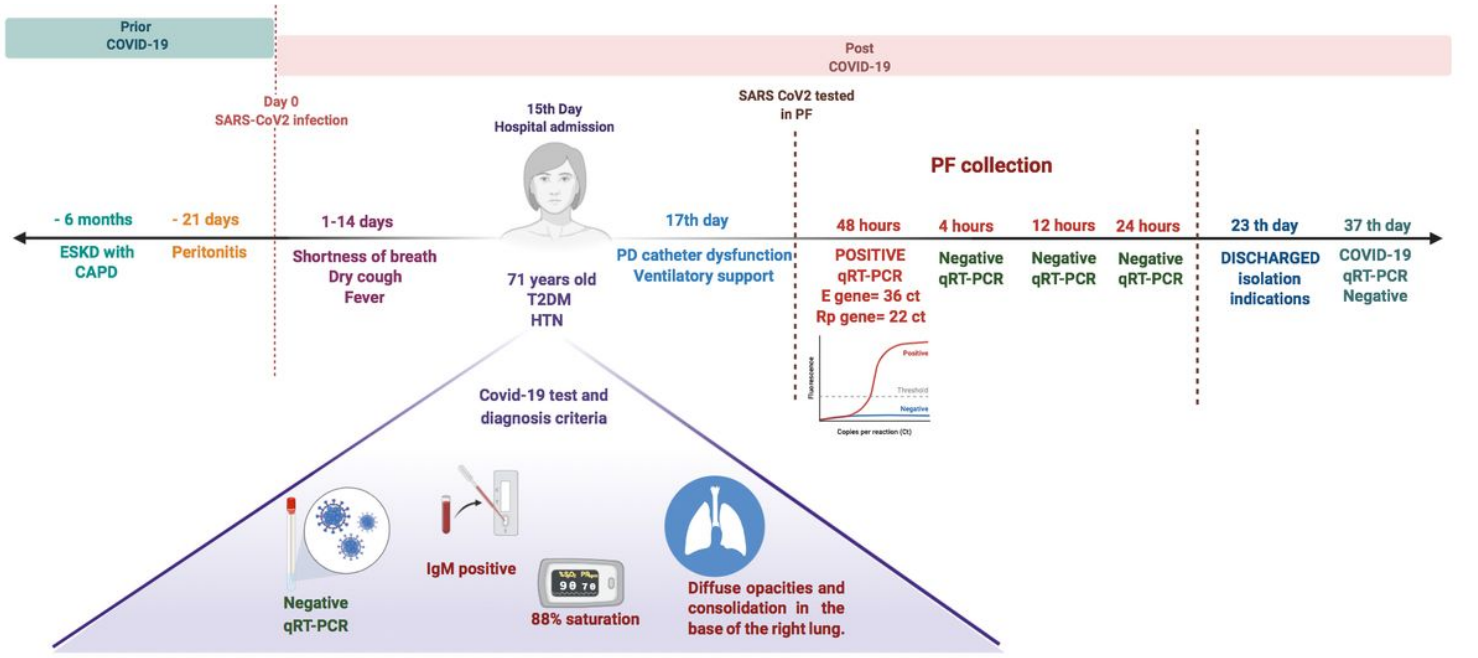
from: https://linkinghub.elsevier.com/retrieve/pii/S0195670120300463

20. La Scola B, Le Bideau M, Andreani J, Hoang VT, Grimaldier C, Colson P, et al. Viral RNA load as determined by cell culture as a management tool for discharge of SARS-CoV-2 patients from infectious disease wards. Eur J Clin Microbiol Infect Dis [Internet]. 2020 Jun 27;39(6):1059–61. Available from: http://link.springer.com/10.1007/s10096-020-03913-9
21. Alexiewicz JM, Smogorzewski M, Fadda GZ, Massry SG. Impaired Phagocytosis in Dialysis Patients: Studies on Mechanisms. Am J Nephrol [Internet]. 1991;11(2):102–11. Available from: https://www.karger.com/Article/FullText/168284
22. Massry SG, Smogorzewski M. Dysfunction of polymorphonuclear leukocytes in uremia: Role of parathyroid hormone. Kidney Int [Internet]. 2001 Feb;59:S195–6. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0085253815477890
23. Betjes MGH. Immune cell dysfunction and inflammation in end-stage renal disease. Nat Rev Nephrol [Internet]. 2013 May 19;9(5):255–65. Available from: http://www.nature.com/articles/nrneph.2013.44
24. Agrawal S, Gollapudi P, Elahimehr R, Pahl M V., Vaziri ND. Effects of end-stage renal disease and haemodialysis on dendritic cell subsets and basal and LPS-stimulated cytokine production. Nephrol Dial Transplant [Internet]. 2010 Mar 1;25(3):737–46. Available from: https://academic.oup.com/ndt/article-lookup/doi/10.1093/ndt/gfp580
25. Vaziri ND, Pahl M V., Crum A, Norris K. Effect of Uremia on Structure and Function of Immune System. J Ren Nutr [Internet]. 2012 Jan;22(1):149–56. Available from: https://linkinghub.elsevier.com/retrieve/pii/S105122761100210X
26. Smogorzewski M, Massry SG. Defects in B-cell function and metabolism in uremia: Role of parathyroid hormone. Kidney Int [Internet]. 2001 Feb;59:S186–9. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0085253815477877
27. Girndt M, Sester M, Sester U, Kaul H, Köhler H. Molecular aspects of T – and B-cell function in uremia. Kidney Int [Internet]. 2001 Feb;59:S206–11. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0085253815477919
28. Pahl M V., Gollapudi S, Sepassi L, Gollapudi P, Elahimehr R, Vaziri ND. Effect of end-stage renal disease on B-lymphocyte subpopulations, IL-7, BAFF and BAFF receptor expression. Nephrol Dial Transplant [Internet]. 2010 Jan 1;25(1):205–12. Available from: https://academic.oup.com/ndt/article-lookup/doi/10.1093/ndt/gfp397
29. Meier P, Spertini F, Blanc E, Burnier M. Oxidized Low-Density Lipoproteins Activate CD4 + T Cell Apoptosis in Patients with End-Stage Renal Disease through Fas Engagement. J Am Soc Nephrol [Internet]. 2007 Jan;18(1):331–42. Available from: http://www.jasn.org/lookup/doi/10.1681/ASN.2006050514
30. Moser B, Roth G, Brunner M, Lilaj T, Deicher R, Wolner E, et al. Aberrant T cell activation and heightened apoptotic turnover in end-stage renal failure patients: a comparative evaluation between

non-dialysis, haemodialysis, and peritoneal dialysis. Biochem Biophys Res Commun [Internet]. 2003 Aug;308(3):581–5. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0006291X03013895

31. Yoon J-W, Gollapudi S, Pahl MV, Vaziri ND. Naïve and central memory T-cell lymphopenia in end-stage renal disease. Kidney Int [Internet]. 2006 Jul;70(2):371–6. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0085253815519339
32. Ikizler TA, Kliger AS. Minimizing the risk of COVID-19 among patients on dialysis. Nat Rev Nephrol [Internet]. 2020 Jun 6;16(6):311–3. Available from: http://www.nature.com/articles/s41581-020-0280-y
33. Gheblawi M, Wang K, Viveiros A, Nguyen Q, Zhong J-C, Turner AJ, et al. Angiotensin-Converting Enzyme 2: SARS-CoV-2 Receptor and Regulator of the Renin-Angiotensin System. Circ Res [Internet]. 2020 May 8;126(10):1456–74. Available from: https://www.ahajournals.org/doi/10.1161/CIRCRESAHA.120.317015

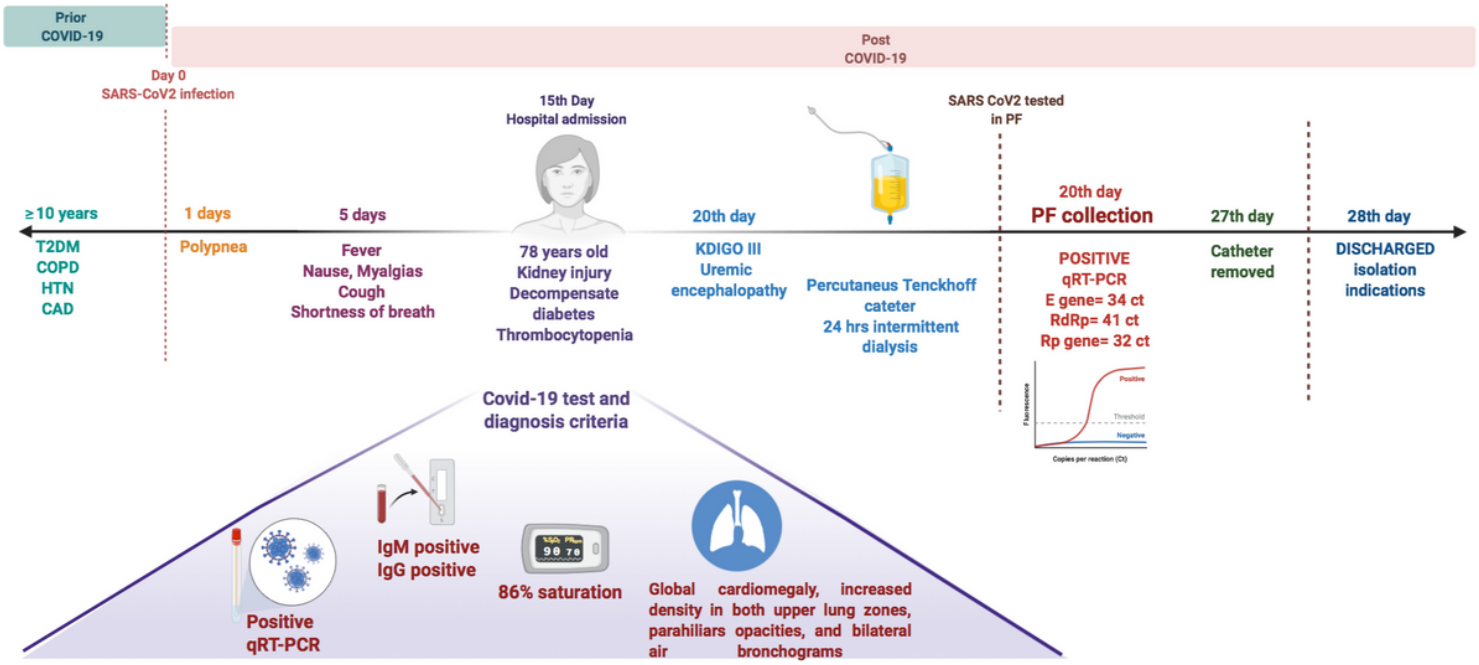
Figures



ESKD, End-stage kidney disease; **CAPD**, continuous ambulatory peritoneal dialysis; **T2DM**, type 2 diabetes mellitus; **HTN**, Hypertension; **PD**, peritoneal dialysis; **PF**, peritoneal fluid; **CT**, cycle threshold; **SARS CoV2**, Severe acute respiratory syndrome coronavirus 2; **qRT-PCR**, quantitative Reverse Transcription-Polymerase Chain Reaction.

Figure 1

Visual Abstract for Case 1. Created with Biorender.com



T2DM, type 2 diabetes mellitus; **COPD**, chronic obstructive pulmonary disease**; HTN,** Hypertension; **CAD** coronary artery disease; **KDIGO**, kidney disease improving global outcome; **PF**, peritoneal fluid; **CT**, cycle threshold; **SARS CoV2**, Severe acute respiratory syndrome coronavirus 2; **qRT-PCR**, quantitative Reverse Transcription-Polymerase Chain Reaction.

Figure 2

Visual Abstract for Case 2. Created with Biorender.com