Recommendations for the prevention, mitigation and containment of the

emerging SARS-CoV-2 (COVID-19) pandemic in haemodialysis centres

^{1,2}Carlo Basile, ³Christian Combe, ⁴Francesco Pizzarelli, ⁵Adrian Covic, ⁶Andrew Davenport,

⁷Mehmet Kanbay, ⁸Dimitrios Kirmizis, ⁹Daniel Schneditz, ¹⁰Frank van der Sande, and ¹¹Sandip Mitra

on behalf of the Eudial Working Group of ERA-EDTA

¹Division of Nephrology, Miulli General Hospital, Acquaviva delle Fonti, Italy

²Associazione Nefrologica Gabriella Sebastio, Martina Franca, Italy

³Service de Néphrologie Transplantation Dialyse Aphérèse, Centre Hospitalier Universitaire de

Bordeaux, France

⁴Nephrology Unit, SM Annunziata Hospital, Florence, Italy

⁵Nephrology Clinic, Dialysis and Renal Transplant Center - 'C.I. Parhon' University Hospital, and

'Grigore T. Popa' University of Medicine, Iasi, Romania

⁶UCL Centre for Nephrology, Royal Free Hospital, Division of Medicine, University College,

London, United Kingdom

⁷Division of Nephrology, Department of Medicine, Koc University School of Medicine, Istanbul,

Turkey

⁸Department of Nephrology, Colchester General Hospital, Essex, United Kingdom

⁹Otto Loewi Research Center, Medical University of Graz, Graz, Austria

¹⁰Department of Internal Medicine, ¹⁰Division of Nephrology, University Hospital Maastricht,

Maastricht, The Netherlands

¹¹Manchester Academy of Health Sciences Centre, Manchester University Hospitals Foundation

Trust and University of Manchester, Oxford Road, Manchester, UK

Carlo Basile ORCID ID: 0000-0001-8152-5471

Francesco Pizzarelli ORCID ID: 0000-0003-0095-953X

Daniel Schneditz ORCID ID: 0000-0002-0124-1012

1

Address for correspondence:

Carlo Basile, MD

Miulli General Hospital

70121 Acquaviva delle Fonti, Italy

Tel + 39-099-4773688

E-mail: basile.miulli@libero.it

KEY WORDS: Coronavirus – COVID-19 - End stage kidney disease - Haemodialysis - Pandemic

ABSTRACT

COVID-19, a disease caused by a novel coronavirus, is a major global human threat which has turned into a pandemic. This novel coronavirus has specifically high comorbidity in the elderly and in comorbid populations. Uraemic patients on dialysis combine an intrinsic fragility and a very frequent burden of comorbidities with a specific setting in which many patients are repeatedly treated in the same area (haemodialysis centres). Moreover, if infected, the intensity of dialysis requiring specialised resources and staff is further complicated by requirements for isolation, control, and prevention, putting healthcare systems under exceptional additional strain. Therefore, all measures to slow if not to eradicate the pandemic and to control unmanageable high incidence rates must be taken very seriously. The aim of the present review of the Eudial Working Group of ERA-EDTA is to provide recommendations for the prevention, mitigation and containment in haemodialysis centres of the emerging COVID-19 pandemic. The management of patients on dialysis affected by COVID-19 must be carried out according to strict protocols to minimize the risk for other patients and personnel taking care of these patients. Measures of prevention, protection, screening, isolation, and distribution have been shown to be efficient in similar settings. They are essential in the management of the pandemic and should be taken in the early stages of the disease.

INTRODUCTION

An epidemic of SARS-CoV-2 (COVID-19), a new strand of the coronavirus family, originated from Wuhan (China) in December 2019; was declared a pandemic by the World Health Organization as of March 11, 2020 (https://www.who.int/emergencies/diseases/novel-coronavirus-2019). The global pandemic of SARS-CoV-2 (COVID-19) is quickly affecting the delivery of health care worldwide (1-4). This novel coronavirus has specifically high comorbidity in the elderly and in comorbid populations (1-4). Chronic kidney disease constitutes a relevant co-morbidity, and dialysis centres pose a risk as potential vector in the spreading of this pandemic (1-4). In previous epidemics or catastrophic situations, the case fatality rate has always been much higher in dialysis patients than in the general population.

In the first two decades of this century, three members of the coronavirus family, SARS-CoV, MERS-CoV and SARS-CoV-2, have caused three major pandemic outbreaks of infectious respiratory diseases. At the present time, it is believed that SARS-CoV-2 is more contagious, but with a lower case fatality rate than the other two viruses. Compared with the previous two outbreaks, the epidemic area of COVID-19 caused by SARS-CoV-2 is larger, the number of infected people and, consequently, the number of deaths higher, and the strain on the healthcare system, as well as the global economic loss greater (1 - 4).

Uraemic patients on dialysis combine an intrinsic fragility and a very frequent burden of comorbidities with a specific setting in which many patients are repeatedly treated in the same area (haemodialysis centres). Dialysis patients constitute a susceptible population because of their older age and their less efficient immune system, and they are therefore more prone to develop severe infectious diseases than the general population (5, 6). Dialysis patients are exposed and re-exposed to a higher contamination risk than the general population because their routine treatment usually requires three dialysis sessions per week. Moreover, if infected, the intensity of dialysis requiring specialised resources and staff is further complicated by requirements for isolation, control, and prevention, putting healthcare systems under exceptional additional strain. Therefore, all measures to

slow if not to eradicate the pandemic and to control unmanageable high incidence rates must be taken very seriously.

To the best of our knowledge, at the time of writing of this paper (March 14, 2020), only one series of cases from one haemodialysis centre in Wuhan has been published (7). The authors reviewed the whole course of the outbreak emerging in the haemodialysis centre of Renmin Hospital, Wuhan University from January 14, 2020, the day the first case was confirmed, to February 17, 2020, the day of the epidemic extinction. Authors reported that 37 cases in 230 haemodialysis patients (16.1%) and four cases out of 33 staff members (12.1%) were diagnosed with COVID-19. Dialysis patients with COVID-19 had less lymphopenia, lower serum levels of inflammatory cytokines, and milder clinical disease than other patients affected by COVID-19 infection. During that epidemic, 7 dialysis patients died, including six with COVID-19 and one without COVID-19. The presumed causes of death were not directly related to pneumonia, but due to cardiovascular and cerebrovascular diseases, and hyperkalaemia. The outcome of the four staff members was favourable (7).

Isolation practices can be effective for preventing secondary transmission of viruses closely related to COVID-19. For instance, during the 2015 MERS-CoV outbreak in Korea, although 116 participants in three haemodialysis units were incidentally exposed to the virus, strict patient surveillance and proper isolation practice prevented secondary transmissions (8).

COVID-19 infection in patients treated in dialysis centres presents a particular challenge as the risk of transmission to the medical staff, to facility workers, to other patients, and to family members is importantly increased.

The Chinese Society of Nephrology (9), the Taiwan Society of Nephrology (10)) and the Centers for Disease Control and Prevention (https://www.cdc.gov/coronavirus/2019-ncov/healthcare-facilities/dialysis.html) have recently developed guidelines for dialysis units during the COVID-19 outbreak. The aim of the present review of the Eudial Working Group of ERA-EDTA is to provide recommendations for the prevention, mitigation and containment in haemodialysis centres of the

emerging SARS-CoV-2 (COVID-19) pandemic. In doing so, we have held in high consideration the suggestions of the Asian colleagues, given their significant experience in dealing with COVID-19 (9, 10), the interim additional guidance released by the Centers for Disease Control and Prevention on March 10, 2020 (11) and the World Health Organization recommendation for the rational use of personal protective equipment for COVID-19 (12). The Eudial Working Group will update its recommendations any time new data and evidences will be available. The ERA-EDTA also launched a dedicated webpage regularly updated https://www.era-edta.org/en/covid-19-news-and-information/

RECOMMENDATIONS

Healthcare team

- A working team consisting of dialysis physicians, nursing staff and technicians should receive training in updated clinical knowledge of the COVID-19 epidemic, epidemic prevention tools, and guidelines from the government, scientific societies and hospital authorities. Instructions should include how to use the different types of facemasks, how to use tissues to cover the nose and mouth when coughing or sneezing, how to dispose of tissues and contaminated items in waste receptacles, and how and when to perform hand hygiene. Training can be done peer to peer or online.
- Latest care recommendations and epidemic information should be updated and delivered to all medical care personnel as needed.
- Staff members should self-monitor their symptoms (if any) and should inform the team leader
 in case they or their family members develop symptom(s) suggestive of COVID-19 infection.
 Sick members of the team should stay at home, and in any case should not be in contact with
 patients or other team members.
- Nurses should be trained to take nasopharynx swabs for COVID-19 PCR, with appropriate
 dressing using a FFP2 mask (filtering 95% of particulate matter and aerosols in inhaled air),
 goggles, mobcap, disposable surgical blouse, and gloves.

Dialysis patients and dialysis facilities

• Dialysis patients should be instructed to stay at home while off dialysis and on their nondialysis days, to use individual transport to and from dialysis facilities, to avoid public transportation, to abstain from travelling around the country, to avoid personal contact and to abstain from public, private, or religious events (family reunions, marriages, funerals, etc.). Parents and grandparents on dialysis may want to abstain from personal contact especially with their children and grandchildren because the younger population serves as a vector of the disease often without showing symptoms.

- Dialysis facilities should provide patients with instructions (in appropriate languages) about hand hygiene, respiratory hygiene, and cough etiquette. Instructions should include how to use facemasks, how to use tissues to cover nose and mouth when coughing or sneezing, how to dispose of, preferably disposable paper, tissues and contaminated items in waste receptacles, and how and when to perform hand hygiene. Dispensers of hydro-alcoholic solutions should be installed in waiting rooms. Patients must be educated and encouraged to perform hand hygiene at least on arrival and at the time of departure from the unit and if in contact with respiratory secretions. Dialysis facilities should have space in waiting areas for ill patients to sit separated from other patients by at least 2 metres. Medically stable patients might opt to wait in a personal vehicle or outside the healthcare facility. Two metres separation between dialysis stations is advisable.
- Treatment and waiting areas should have good air conditioning and ventilation to remove particles and aerosol droplets from the air.
- Body temperature should be systematically measured before the start and at the end of the dialysis session in all patients.
- Early recognition and isolation of individuals with respiratory infection is mandatory: 1. dialysis facilities should identify patients with signs and symptoms of fever, cough, upper airway involvement or conjunctivitis <u>before</u> they enter the waiting room and treatment area; 2. patients must inform staff of fever or respiratory symptoms before arrival at the facility by phone or appropriate electronic means; thus, the facility can be prepared for their arrival (preferably they should be seen on a first aid department and not on a dialysis department) or triage them to a more appropriate setting such as an acute care hospital; 3. patients with respiratory symptoms should be brought to an appropriate treatment area as soon as possible

in order to minimize the time in waiting areas; 4. all patients who have fever, cough, upper airway involvement or conjunctivitis should be screened for novel Coronavirus infection. For sampling, patients should be either in a single-patient room, or in a room dedicated to sampling. Disinfection of the room after sampling is mandatory.

- Ideally, symptomatic patients should be dialyzed in a separate isolation room (if available), in which a negative pressure atmosphere can be established, with the door closed. Otherwise, they should wait in a separate isolation room and receive dialysis in the last shift of the day until infection is excluded. He/she should wear a proper (surgical or N95) mask filtering 95% of the particulate matter smaller than 2.5 μm in the aerosol of exhaled air.
- Patients with confirmed COVID-19 infection should be admitted to an airborne infection isolation room and should not receive dialysis in an outpatient dialysis facility, unless an airborne infection isolation room is available. All personnel involved in the direct care of patients affected by COVID-19 must undertake full protection, including long-sleeved waterproof isolation clothing, hair caps, goggles, gloves and medical masks (FFP2 or FFP3 mask if available) filtering 95 to 99% of particulate matter and aerosols in inhaled air. Hand hygiene must be strictly implemented, carefully washing hands with soap and water and systematically using alcoholic solutions and disposable gloves.
- Consideration should be given to cohorting more than one patient with suspected or confirmed COVID-19 and the healthcare team caring for them in the same section of the unit and/or on the same shift (e.g., consider the last shift of the day). Avoid, however, mixing of suspected and confirmed cases.
- Manpower should be cohorted in separate teams for the management of high-risk and low-risk patients. Only the assigned healthcare team should enter the isolation room/cohort area, all non-scheduled team-mates should be excluded at all times.

- If a newly confirmed or highly suspected case of novel coronavirus infection in dialysis centres is identified, disinfection must be carried out immediately. Areas in close contact with these patients must not be used for other patients until cleared.
- The medical waste from confirmed or suspected patients with novel coronavirus infection must be considered as infectious medical waste and disposed accordingly.

Duration of isolation precautions for patients under investigation for or with confirmed COVID-19

- Discontinuation of isolation precautions should be determined on a case-by-case basis, in conjunction with local, state, and federal health authorities, until information is available regarding viral shedding after clinical improvement.
- Factors to be considered include: presence of symptoms related to COVID-19 infection, date when symptoms resolved, other conditions that require specific precautions (e.g., tuberculosis, Clostridium difficile), other laboratory information reflecting clinical status, alternatives to inpatient isolation, such as the possibility of safe recovery at home.

Surgical operations

Patients who need vascular access surgery should be screened for COVID-19. Operations on
patients with confirmed or suspected COVID-19 infection must be carried out in a designated
room with necessary protection for medical staff.

Operational strategies for family members and caregivers

All family members living with dialysis patients must follow all precautions and regulations
given to patients to prevent person-to-person and within family transmission of the COVID19, which include body temperature measurement, good personal hygiene, handwashing, and
prompt reporting of potentially infected individuals.

- Dialysis patients, who have a family member or caregiver subject to quarantine (precautionary isolation basically for 14 days because of a potential exposition to the coronavirus but not showing any signs of infection) (13), can have dialysis as usual during the 14-day period of quarantine of the family members or caregivers.
- Once family members or caregivers of dialysis patients have been converted to a confirmed
 case, the patient's identity must be upgraded and treated in accordance with the abovementioned conditions.

Home haemodialysis and peritoneal dialysis

These patients should be assisted at home as far as is possible, using telereporting assistance
or other electronic systems for clinical management and to supplement home visits by
healthcare staff, as deemed necessary.

CONCLUSIONS

COVID-19, a disease caused by a novel coronavirus, is a major global human threat which has turned into a pandemic. The only study so far reporting an outbreak of COVID-19 in a dialysis centre indicates that dialysis patients are a highly susceptible population and haemodialysis centres are a high-risk area in the outbreak of a COVID-19 epidemic (7). The management of patients on dialysis affected by COVID-19 must be carried out according to strict protocols to minimize the risk for other patients and personnel taking care of these patients. Measures of prevention, protection, screening, isolation, and distribution have been shown to be efficient in similar settings (8). Prevention plays a key role; the other measures are essential in the mitigation and containment of the COVID-19 pandemic in haemodialysis centres.

Conflict of interest statement

The authors have no conflicts of interest related to this manuscript.

REFERENCES

- 1. Zhu N, Zhang D, Wang W, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *N Engl J Med* 2020 Feb 20; 382(8): 727 733
- 2. Mahase, E. Coronavirus covid-19 has killed more people than SARS and MERS combined, despite lower case fatality rate. *BMJ* 2020 Feb 18; 368: m641
- 3. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet* 2020 Feb 15; 395(10223): 497 506
- 4. Naicker S, Yang CW, Hwang SJ, et al, The Novel Coronavirus 2019 Epidemic and Kidneys. *Kidney Int* 2020 doi: https://doi.org/10.1016/j.kint.2020.03.001
- 5. Syed-Ahmed M, Narayanan M. Immune Dysfunction and Risk of Infection in Chronic Kidney Disease. *Adv Chronic Kidney Dis* 2019 Jan 26(1): 8 15
- 6. Betjes MG. Immune cell dysfunction and inflammation in end-stage renal disease. *Nat Rev Nephrol* 2013 May 9(5): 255 265
- 7. Ma Y, Diao B, Lv X, et al. 2019 novel coronavirus disease in hemodialysis (HD) patients: Report from one HD center in Wuhan, China. Available at https://www.medrxiv.org/content/10.1101/2020.02.24.20027201v2 Accessed 14 March 2020
- 8. Park HC, Lee SH, Kim J, et al. Effect of isolation practice on the transmission of middle east respiratory syndrome coronavirus among hemodialysis patients: A 2-year prospective cohort study. *Medicine* (Baltimore) 2020 Jan; 99(3): e18782
- 9. Chinese Society of Nephrology. Recommendations for prevention and control of new coronavirus infection in blood purification center (room) (First trial version). Chinese Society of Nephrology, 2 March 2020
- 10. Hwang S-J. Guideline for dialysis facilities during COVID-19 outbreak, Taiwan Society of Nephrology, 16 February 2020
- 11. Centers for Disease Control and Prevention. Interim Additional Guidance for Infection Prevention and Control Recommendations for Patients with Suspected or Confirmed COVID-19 in Outpatient Hemodialysis Facilities at https://www.cdc.gov/coronavirus/2019-ncov/healthcare-facilities/dialysis.html released on March 10, 2020
- 12. World Health Organization. Rational use of personal protective equipment for coronavirus disease (COVID-19): interim guidance released on 27 February 2020
- 13. Lauer SA, Grantz KH, Jones FK, et al. The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application. *Ann Intern Med* 2020 Mar 10. doi: 10.7326/M20-0504