Role of Screening for COVID-19 in Hemodialysis Wards, Results of a Single Center Study

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Introduction. Seven months after the emergence of SARS-COV-2 virus, there is paucity of data regarding the epidemiology of the virus in hemodialysis patients. We aim to present the results of the screening program implied after outbreak of COVID-19 in a referral hemodialysis ward.

Methods. We started clinical screening and obligatory mask wearing for dialysis patients and personnel on 20-Feb-2020. However 11 symptomatic COVID-19 patients emerged till day +36. On days +39 and +40 a screening program was implied including measurement of SARS-COV-2 PCR and immunoglobulin G and M (IgG/IgM) and chest computerized tomography (CT) scan. The results of chest CT scan, classified according to the coronavirus disease 2019 (COVID-19) Reporting and Data System (CO-RADS) classification; as with very low (grade 1-normal), low, indeterminate, high, and very high likelihood of COVID-19 (grades 2, 3, 4, and 5; respectively), were used for compartmentalization of patients.

Results. Among 178 patients (68.2% male, mean age = 58.7 ± 16.6 years), 11 got COVID-19 before screening, two of whom died. Chest CT scans were normal in 71.3% and grade 2, 3, 4, and 5 in 7.9%, 4.5%, 5.6%, and 10.7%; respectively. PCR and IgG and/or IgM were positive in 27 and 32 patients. Eighty-three patients had evidence of COVID-19 infection, who were significantly older (62.2 ± 16.6 vs. 56.1 ± 16.02, $P < .05$). There was no difference in the rate of infection considering gender, diabetes mellitus, hypertension and different blood groups.

Conclusion. Asymptomatic SARS- COV 2 infection may affect a large number of dialysis patients. We highly recommend a screening strategy whenever the number of patients is increasing.

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INTRODUCTION

In December 2019, a cluster of patients with pneumonia of unknown cause was diagnosed in Wuhan, China, later attributed to a novel corona virus, named 2019-nCoV.[1] Different from both MERS-CoV and SARS-CoV, 2019-nCoV is the seventh member of the family of corona viruses that infect humans.[1] Since then, with disease spread throughout the world, as of 31st July 2020, 17,106,007 confirmed cases of COVID-19, i.e. the Corona virus disease 2019 caused by SARS-CoV-2 virus, and 668,910 deaths have been reported to World Health Organization (WHO).[2,3] In our country, Iran, a total of 301,530 confirmed cases and 16,569 confirmed deaths have been recorded at the time of this writing, since the first reports

of disease emergence at February 2020.[4,5]

Epidemiologic studies suggest a higher susceptibility of patients with underlying comorbidities such as diabetes, hypertension, cardiovascular disease and elderly.[6,7] However due to the new emergence of SARS-COV-2 virus there is a lack of reliable data on the epidemiology and behavior of disease in different groups of patients, specially chronic hemodialysis (HD) patients. These patients have a general state of immunosuppression, due to uremic state, that contributes to high prevalence of infections.[8] On the other hand they are susceptible to infections due to frequent travels to dialysis wards, exposure to clusters of other patients and medical staff and frequent touch for cannulations and other stages of dialysis delivery.

Among the numerous papers that have been published within the past few months on COVID-19, there are few reports on COVID-19 epidemiology in chronic dialysis patients. Hence, in this paper, we present the actions undertaken and the incidence of COVID-19 in patients and health staff of a large referral HD ward, with over 3000 dialysis sessions per month, as a diary.

MATERIALS AND METHODS

On 20th February 2020, with official declaration of COVID-19 entry into Iran, we started clinical screening for dialysis patients and personnel and obligatory wearing of surgical masks for personnel throughout their working hours, together with hand-washing upon entrance for the patients and restrictions on entry of patients' accompanies. On 21th Feb (day +1) the first dialysis patient with COVID-19 was diagnosed and admitted in another hospital, who unfortunately died after 6 days. On day 3 another patient, who complained of fever was assessed by the COVID-19 unit of the hospital, who had normal complete blood count (CBC) and chest X ray and was not diagnosed with COVID-19. However despite stopping of fever after 24 hours, he developed diarrhea and nausea, and was admitted in the designated COVID-19 ward of the hospital with lymphopenia and positive Chest computerized tomography (CT) scan with diagnosis of COVID-19, later confirmed by positive polymerase chain reaction (PCR) test. Subsequently, 1 more patient was diagnosed with COVID-19 within a week. At this time (day +7) wearing of surgical masks became obligatory for all patients, personnel were obliged to wear complete personal protective equipments (PPEs) (Hazmat suits, N95 masks, face shields or goggles and gloves) and hemodialysis shifts were reduced to twice a week in about 60% of patients, who had interdialytic weight gain less than 3 kg and pre-dialysis serum potassium level below 5.5 meq/L, to reduce the risk of infection due to frequency of travels to and contacts in the dialysis ward with cautions given for symptoms of volume overload and instructions for strict diet control. Screening was augmented from temperature measurement to complete history taking at entry to dialysis ward, for any symptoms of viral infection (cough, sore throat, headache, dyspnea, nausea, vomiting, diarrhea, malaise, and anosmia) and history of COVID-19 in close contacts or travel to epicentres (at that time, the cities of Qom, Rasht and Gorgan). Food ingestion was forbidden during dialysis, the dialysis restaurant was closed and take home food packages were distributed. Despite these strict isolation measures, the number of symptomatic COVID-19 patients rose to 11 at day +36.

So on day +39 the hospital declared a state of emergency for hemodialysis ward and a screening strategy was planned on days +39 and +40 for all patients before entering the dialysis ward, which included measurement of complete blood count (CBC) and white blood cell differentiation, C-reactive protein (CRP), SARS- COV- 2 PCR, and chest CT scan.

The results of chest CT scan were assumed as the most sensitive screening modality and were studied on line by the radiologist of the team (B), according to the result of which patients were designated to be dialyzed in different rooms by the head of dialysis ward. The chest CT scan results were classified according to the Coronavirus disease 2019 (COVID-19) Reporting and Data System (CO-RADS) classification, as CT scan with very low (grade 1-normal), low, indeterminate, high, and very high likelihood of COVID-19 (grades 2, 3, 4, and 5; respectively) (Table 1).[9] All chest CT scans were performed with Dual Slice CT Scan (Hi Speed NX/I Dual Slice, GE, USA) using a low-dose non-contrast CT scan protocol, with 3 mm gapless slice thickness in full inspiration with the patient in supine position.

Subsequently when the results of CBC, CRP,

Table 1. Chest CT scan Findings

		Likelihood of COVID-19 Infection
CO-RADS 0	CT scan is un-interpretable	-
CO-RADS 1	Normal CT scan or Unequivocal Non-infectious Findings on CT scan	Very Low
CO-RADS 2	Finding of Pulmonary Infectious that is Inconsistent with COVID-19	Low
CO-RADS 3	Equivocal CT scan Findings that are also Found in other Viral Pneumonias or Non-infectious Conditions	Indeterminate
CO-RADS 4	Typical CT scan Findings of COVID-19 but in Central or Unilateral Distribution	High
CO-RADS 5	Multifocal, Bilateral, Sub-pleural Typical CT scan Findings of COVID-19	Very High
CO-RADS 6	Confirmation CT scan Finding with Positive RT-PCR Test*	Definitive

Dutch Association for Radiology (Nederlandse Vereniging voor Radiologie, NVvR). https://www.radiologen.nl/secties/netwerk-covid-19/documenten/handreiking-standaardverslag-ct-thorax-covid-inclusief-co-rads. (in Dutch) [accessed 14 April 2020].
*Reverse transcriptase polymerase chain reaction

and PCR were obtained on the following days, further decisions for compartmentalization of patients were made.

After 1 month of the screening program, kits for measurement if serum Immunoglobulin G and M (IgG and IgM) of SARS-CoV-2 virus became available, and the serology test was performed for all patients.

The SARS-CoV-2 detection was done by real-time reverse transcriptase polymerase chain reaction (RT-PCR) through nasopharyngeal swab samples of participants for SARS-CoV-2 test. The swabs and tissue samples were placed in viral transport medium or sterile saline and kept refrigerated until sent to the laboratory to be processed within 4-12 hours of collection. The COVID-19 One-Step RT-PCR Kit (Pishtaz Teb Diagnostics, Iran) was used for detection of Corona virus, and the antibodies were measured with the ELISA kit of Pishtaz Teb Diagnostics, Iran.

Radiologic Findings on Chest CT Scan

The CT scan findings of COVID-19 were defined according to the four categories of consensus statement of the Radiological Society of North America (RSNA) endorsed by the Society of Thoracic Radiology and the American College of Radiology (ACR)[10] (Figures 1 to 6). Then the findings were classified to CO-RADS grades as mentioned above and in Table 1.

Typical Appearance

1. Peripheral, bilateral, ground glass opacities ± consolidation or visible intralobular lines ("crazy paving" pattern)
2. Multifocal ground glass opacities of rounded morphology ± consolidation or visible intralobular lines ("crazy paving" pattern)
3. Reverse halo sign or other findings of organizing pneumonia

Indeterminate Appearance

Absence of typical CT findings and the presence of:

1. Multifocal, diffuse, perihilar, or unilateral ground glass opacities ± consolidation lacking a specific distribution and non-rounded or non-peripheral
2. Few very small ground glass opacities with a non-rounded and non-peripheral distribution

Atypical Appearance

Absence of typical or indeterminate features and the presence of:

1. Isolated lobar or segmental consolidation without ground glass opacities
2. Discrete small nodules (e.g. centrilobular, tree-in-bud)
3. Lung cavitation
4. Smoother interlobular septal thickening with pleural effusion

Negative for Pneumonia

No CT scan features to suggest pneumonia, in particular, absent ground glass opacities and consolidation

RESULTS

There were 178 patients, with a mean age of 58.7 ± 16.6, and 68.2% male. The most frequent cause of ESKD was diabetes mellitus, followed by hypertension, polycystic kidney disease, stone disease and glomerulonephritis (Table 2).

Eleven patients had got COVID-19 before the

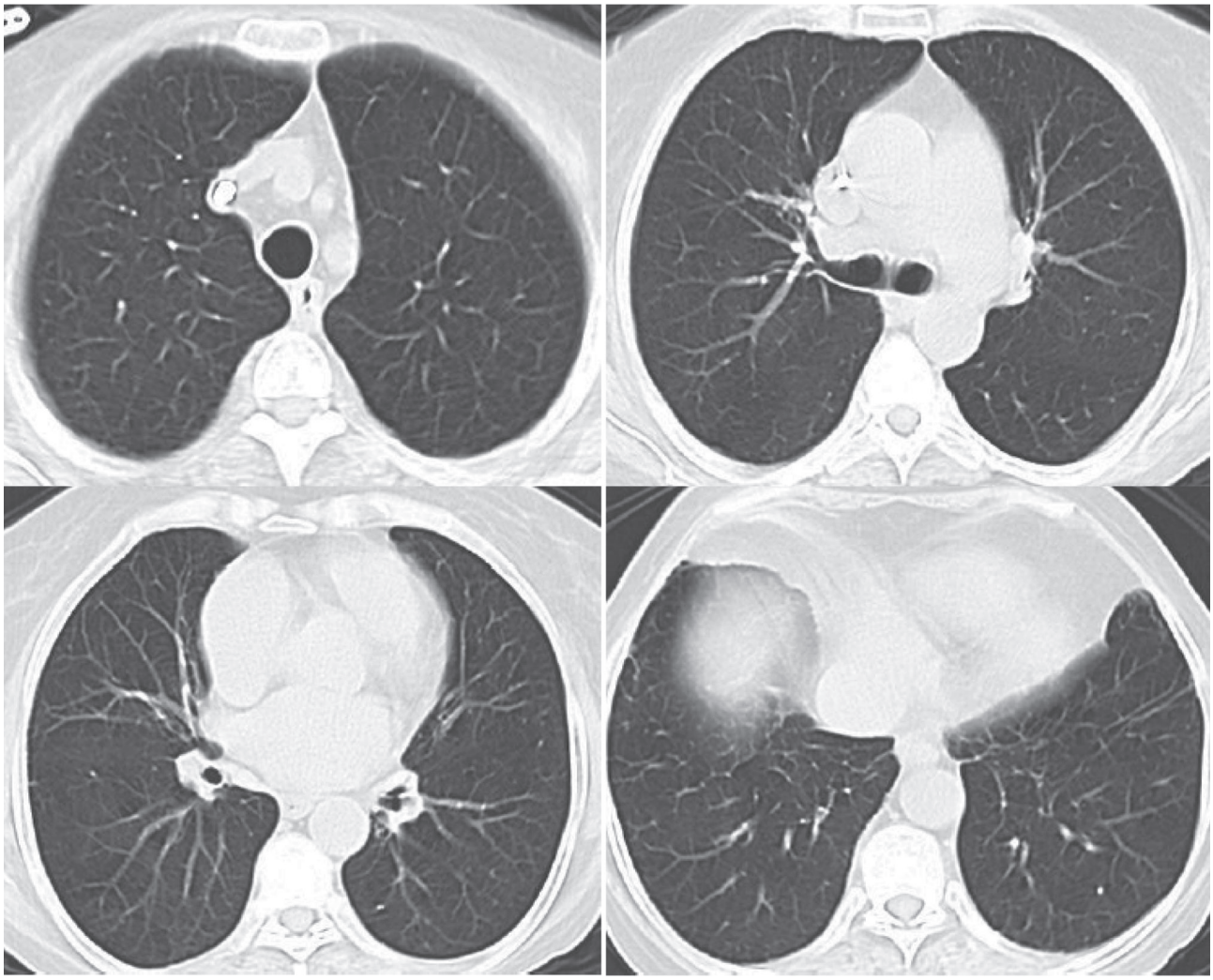

Figure 1. CO-RADS 1 (Normal Lung CT Scan)

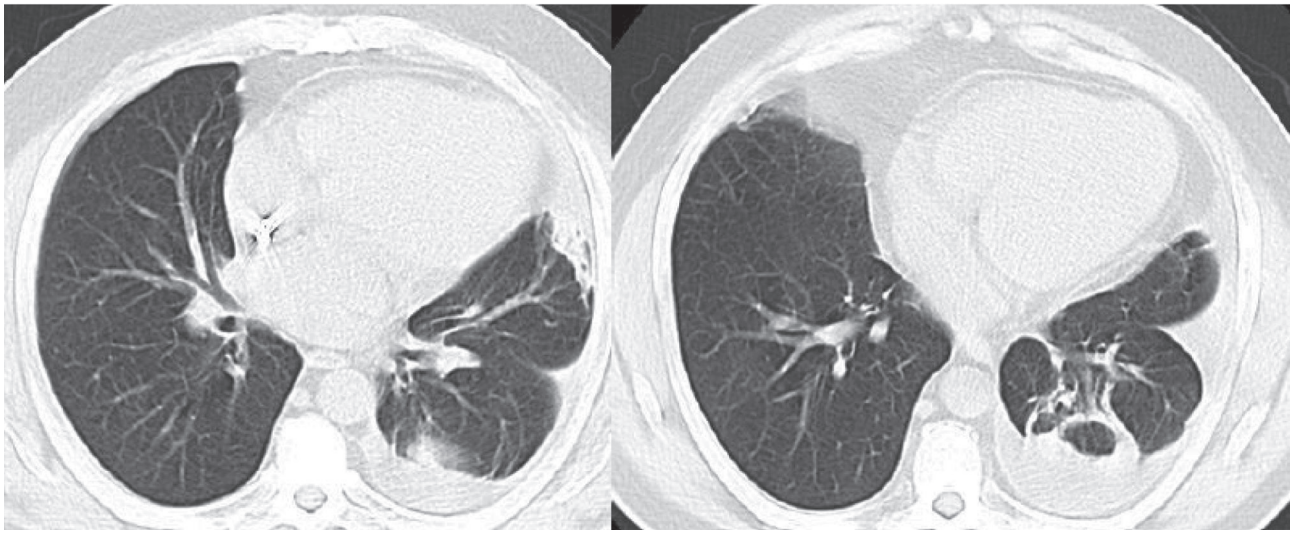

Figure 2. CO-RADS 1 (Pleural Thickening with Fibrotic Changes & Round Atelectasis)

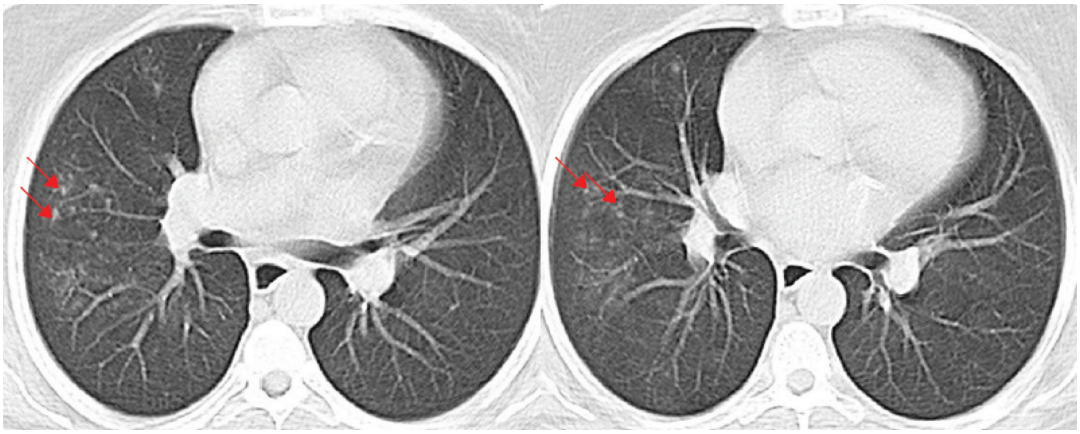

Figure 3. CO-RADS 2 (Tree-in-bud Sign)

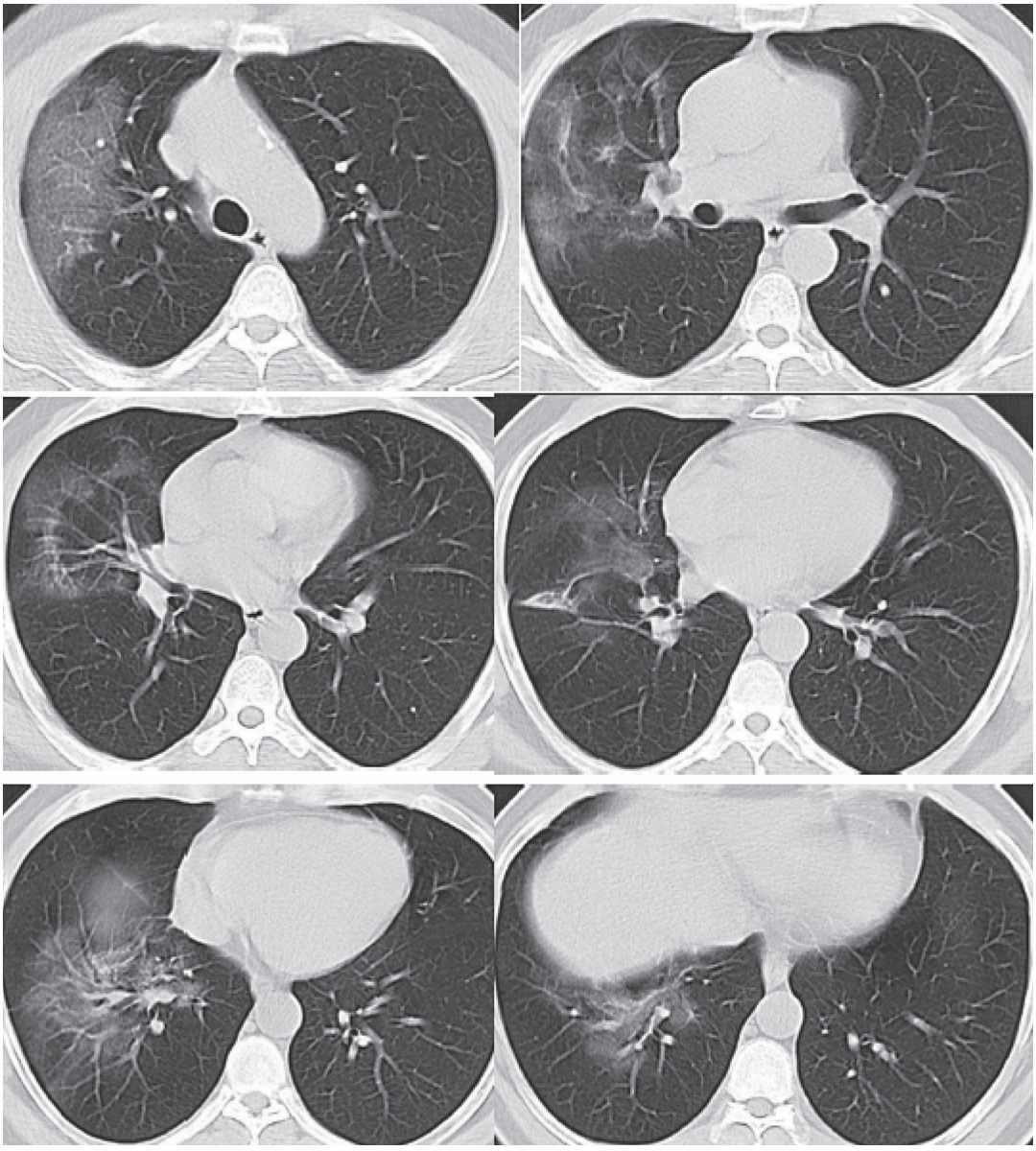

Figure 4. CO-RADS 3 (Unilateral, Homogenous, Extensive Ground Glass Opacities)

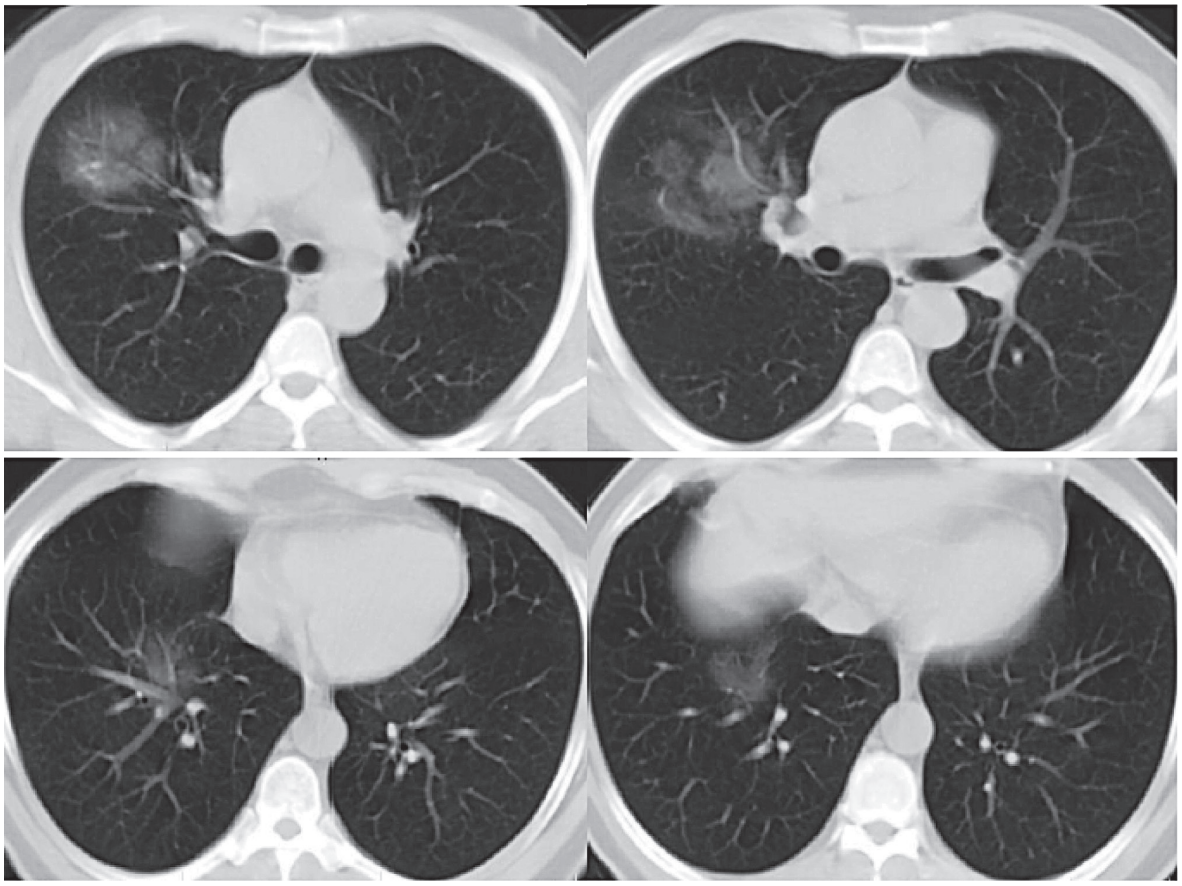

Figure 5. CO-RADS 4 (Unilateral, Central Ground-glass Opacities with or Predominant Peribronchovascular Distribution)

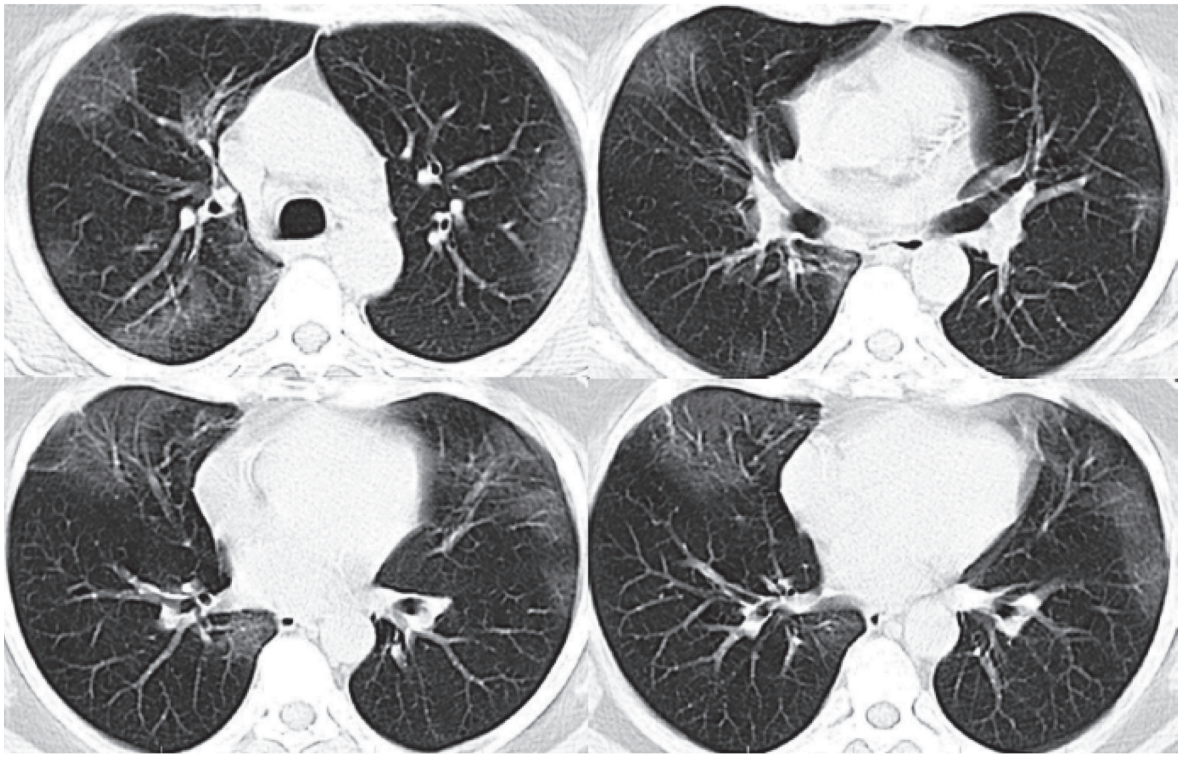

Figure 6. CO-RADS 5 (Subpleural, Multifocal, Bilateral Ground-glass Opacities)

Table 2. Demographic Characteristics of 178 Hemodialysis Patients

Gender, no (%)	
Male	122 (68)
Mean age, y ± SD (range)	58.9 ± 16.5 (22 to 99)
Dialysis Vintage, mo ± SD	143.41 ± 175.2
Primary Disease (%)	
Diabetes Mellitus	30
Hypertension	12.9
Glomerulonephritis	4.5

Table 3. Frequency of Different Evidence of COVID-19 Among 178 Patients (number (%))

No Evidence	111 (62.4%)
Chest CT scan and/or PCR* Evidence	67 (37.6%)
Chest CT scan Only	40 (22.5%)
PCR Only	16 (9%)
Both	11 (6.2%)
Positive PCR	
Negative	151 (84.8%)
Positive	27 (15.2%)
Corona Findings in Chest CT Scan	
Normal (CO-RADS 1)	127 (71.3%)
Positive	51 (28.7%)
Low Suspicious (CO-RADS 2)	14 (7.9%)
Indeterminate Suspicion (CO-RADS 3)	8 (4.5%)
High Suspicion (CO-RADS 4)	10 (5.6%)
Very Highly Suspicious (CO-RADS 5)	19 (10.7%)
Detection Time	
Before Screening (Symptomatic)	11 (16.4%)
After Screening (Asymptomatic)	56 (83.6%)

*Polymerase chain reaction

screening plan including 8 male (72.7%) and 3 female patients, with a mean age of 58.5 ± 8.5 year. The most frequent symptoms and signs were fever and cough (each in 8 patients), followed by dyspnea (7), chills (7), malaise (5), diarrhea (4), myalgia (2), nausea and vomiting (2), headache (1). Two of the symptomatic patients (1 female (58.3 years old) and 1 male (45.3 years old)) died with respiratory failure both after 6 days of admission. All of the eleven symptomatic patients had typical Chest CT scans for viral pneumonia, 6 had positive PCR test, 8 had lymphopenia (lymphocyte count less than 1500) (data not available in 2) and 8 had positive IgG after 1 to 2.5 months of disease start (2 died and could not be tested). Serum IgM was negative in 6 patients and positive in 3 patients after 50, 37, and 37 days of the initiation of symptoms and missing in the two dead patients. Both IgM and IgG were negative in 3 patients.

Overall, chest CT scans were reported as with very low likelihood (CO-RADS 1) in 126 patients (71.3%), assumed as normal CT scan, with low likelihood (CO-RADS 2) in 14 patients, (7.9%), with indeterminate likelihood (CO-RADS 3) in 8 (4.5%), with high likelihood (CO-RADS 4) in 10 (5.6%), and with very high likelihood (CO-RADS 5) in 19 (10.7%) of the patients (Table 3). All 11 symptomatic patients had typical pulmonary changes of viral pneumonia compatible with COVID-19 (CO-RADS 5) and the other 8 typical CT scans were found during screening of asymptomatic patients.

PCR was positive in 27 patients (6 in symptomatic patients and 21 detected after screening).

Lymphopenia, defined as lymphocyte count less than 1500/ µL was found in 92 (51.7%) of dialysis patients and was significantly more frequent in those with positive CT scan only (76.3%), or both CT and PCR positive (70%) compared to patients with only PCR positive (40%) ($P < .05$). The odds of having lymphopenia < 1500 was 3.80 (1.64 to 8.78) in patients with only positive CT scan, 2.75 (0.67 to 11.2) in patients with both CT scan and PCR positive and 0.78 (0.26 to 2.63) in patients with only positive PCR.

After a month of the screening plan, IgG and IgM antibody measurement became available in our hospital and was measured in all patients. IgG was positive in 29, with 8 concurrent positive IgM tests, IgM was positive in 11 (in 3 of whom IgG was negative). These patients were labeled as active or previous COVID-19 patients and dialyzed in different sections.

Overall 32 patients had positive serology (positive IgG, IgM, or both), 16 of whom had concurrent evidence of COVID-19 by other methods. Sixteen did not have any other evidence and we added them to the previous 67, which made 83 probably infected patients detected via chest CT scan, PCR and/or serologic evidence of SAR-COV 2 infection.

Patients with evidence of COVID-19 were significantly older that those with no evidence of the disease (62.2 ± 16.6 vs. 56.1 ± 16.02, $P < .05$).

There was no difference between the rate of infection in male vs. female patients (47.5% vs. 44.6%, $P > .05$), diabetic vs. non-diabetic patients (43.6% vs. 47.9%, $P > .05$), hypertensive vs. non-hypertensive patients (47.8% vs. 45.8%, $P > .05$), and different blood groups ($P > .05$). The rate of

positive antibody test was 26.3% among patients detected with chest CT scan, (OR = 1.94, CI: 0.79 to 4.96), 13% among patients detected by positive PCR (OR = 0.83, CI: 0.17 to 4.06), and 44% among patients detected by both methods (OR = 4.35, CI: 1.05 to 17.97) (*P* for all > .05).

After the screening program 3 of the infected patients became overtly sick, one of whom died and on months 4 to 6, five more patients from non-COVID shifts became sick, 1 of whom died. So the overall mortality rate has been 4/178 (2.2%) and the case fatality rate has been 4/88 (4.5%), among all presumably infected patients and 4/19 (21%) among symptomatic patients, during 6 months.

Three asymptomatic personnel (2 nurses and 1 personal support worker) became PCR positive during screening and the 4th and 5th ones became symptomatic on days 125 and 140. All of them recovered uneventfully.

DISCUSSION

COVID-19 is the Corona virus disease 2019 caused by SARS-CoV-2 virus that was introduced by this name by the WHO director on February 11, 2020. Since then numerous reports of the clinical, epidemiologic and therapeutic presentations of the disease have been published in the literature. However there is a paucity of data regarding COVID-19 in hemodialysis patients, as a susceptible group of patients for infectious diseases. Dialysis patients have a flail immunologic system and are prone to many infections.[8] In addition to that with regular weekly travels to the dialysis units, relatively low social distancing in the wards and common dialysis nurses or technicians and dialysis facilities (mainly the dialysis beds and machines), they can be assumed as a group at risk of for infection with SARS-CoV-2 and possibly further complications.

There are a number of regulations for prevention of spread of viral infections in dialysis units. Generally rigorous precautionary measures are followed for hepatitis B positive patients in dialysis units together with machine segregation and avoidance of reuse.[11,12] For hepatitis C generally machine segregation is not recommended, though a number of studies have shown disease spread between hepatitis C patients in dialysis units.[13-5] Also routine isolation or dedicated machines for HIV-positive patients is not recommended by the Centers for Disease Control and Prevention (CDC), though outbreaks of patient-to-patient HIV transmission have occurred in a number of hemodialysis units throughout the world.[16,17]

Regarding the novel Corona virus, the main instructions for dialysis units given by CDC and American Society of Nephrology are screening with questions on arrival regarding the existence of fever, new cough, or dyspnea, and contact with infected people or travel through areas with high incidence of infection; patient placement in separate rooms, or if unavailable, in isolated shifts or a designated COVID-19 facility; use of face mask by the patients, and employment of standard contact and droplet precautions, including isolation gowns, gloves, masks, and eye protection (shields or goggles) for the personnel and routine disinfection practices including disinfection wipes for the dialysis machine, chair, and all dialysis station surfaces (e.g., the chair side).[18-20]

There is not much data available regarding laboratory and/or imaging screening of asymptomatic hemodialysis patients for Corona virus infection. A study on hemodialysis patients in a hemodialysis center in Wuhan, china, reported 37 cases of COVID-19 among 230 HD patients (16.09%) and 4 cases among 33 staff (12.1%) from January 14th to February 17th, 2020, and no cases afterwards.[21] They found that upgrading level of prevention and protection and later, the universal screening, isolating, and distributing the infected cases, were effective in the epidemic control. They found a very lower proportion of T cells, T helper cells, killer T cells, NK cells and B lymphocytes in peripheral blood mononuclear cells of HD patients compared with that of non-HD patients and even a more decreased number of cells in HD patients with SARS-CoV-2 infection.[21]

In a screening program on 90 regular HD patients in Madrid, 41.1% had COVID-19, of whom 45.9% were diagnosed through symptoms, and 40.5% through subsequent screening.[22] Fever was the most frequent symptom, 50% had lymphopenia and 18.4% had O_2 saturation bellow 95%. Sixteen patients (43.2%) required hospital admission and 6 (16.2%) died. They found a cluster of infection per shift and also among those using public transport. Also a high percentage of staff were involved, and 20% required sick leave.

In our screening program we found 83 definite or

probable infected patients in the first 3 months, i.e., 46% of patients, 14 of whom became symptomatic with 3 deaths. Later we had 5 new cases with 1 death. Among 35 personnel we had 5 PCR positive cases (14.2%), 2 of whom were mildly symptomatic. So our overall infection rate was close to that of the Madrid experience and higher than the Wuhan experience, and our mortality rate was similar to both experiences. Our staff infection rate was close to Wuhan and lower than Madrid, probably due to better preventive measures.

We analyzed the possible reasons for disease spread in our ward, despite implication of strict mask wearing and hand washing practices for the patients and PPE wearing for the personnel, from the early days of the outbreak. We noticed that some of the dialysis beds had clusters of COVID-19 positive patients. Also there were a number of infected patients dialyzed by one nurse, who later turned out to have a positive SARS-Cov 2 PCR test during screening. Seemingly the disinfection protocol (regular changing of the bed sheets, and disinfection of the dialysis machine surfaces, chair-side, bed tables and closets with chlorhexidine and alcohol solutions after each shift) was not enough. We insisted on whole dialysis chair disinfection after each shift and added rinsing of the dialysis chairs with water and detergent in addition to the chlorhexidin and alcohol disinfection protocol, after the shifts of infected patients. Also strict compartmentalization of symptomatic and asymptomatic patients was done, that has been continued till now.

We conclude that, despite screening for COVID-19 symptoms and separation of suspicious patients in other units or shifts, SARS- COV 2 infection may asymptomatically affect a large number of dialysis patients. We highly recommend close monitoring of disinfection strategies, social distancing inside and outside the ward, including for the accompanies, and general screening strategy whenever the number of patients is increasing.

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