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Weekly Rapid Antigen Test Screening for COVID-19 in Patients on Hemodialysis

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Abstract. *Background/Aim: COVID-19 is a concerning issue among in-center hemodialysis (HD) patients. To prevent COVID-19 diffusion in our HD facility, weekly rapid nasal antigen test screening was performed for all asymptomatic patients on chronic HD. This study aimed to assess the performance of weekly rapid antigen test in detecting SARS-CoV-2 infection among asymptomatic patients receiving HD. Patients and Methods: A retrospective analysis was conducted in HD patients who underwent rapid antigen test screening from December 2021 to March 2022. The diagnosis of COVID-19 with rapid antigen test was always confirmed by reverse transcriptase-polymerase chain reaction (RT-PCR). Results: During the observational period, 1,748 rapid antigen tests were performed in 220 HD patients. Mean age was 68.4±14.6 years. Fifteen (8.5%) patients resulted positive for SARS-CoV-2 infection using rapid antigen tests. The diagnosis was subsequently confirmed in 14 (93.3%) patients by RT-PCR. During the same period, 12 (5.4%) symptomatic patients, regularly screened with weekly rapid antigen test, resulted positive for SARS-CoV-2 infection using RT-PCR. Overall, weekly rapid antigen test screening identified 14 out of 26 (53.8%) COVID-19 cases and showed a positive predictive value of 93%. Conclusion: Weekly antigen test screening of asymptomatic patients on chronic HD detected around half of the COVID-19 cases in our population.*

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Key Words: Rapid antigen test, COVID-19, hemodialysis, screening, dialysis, COVID-19 testing, polymerase chain reaction, SARS-CoV-2, coronavirus, PCR.

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Patients on maintenance hemodialysis (HD) are a subset of the population extremely susceptible to the severe consequences of COVID-19. Advanced age, high prevalence of diabetes and cardiovascular disease, as well as immunosuppression due to end-stage kidney disease, are the main determinants of poor outcomes in this population (1-5). Patients on in-center HD also carry a significant risk of contracting SARS-CoV-2 infection, as they may share with potentially infected subjects enclosed spaces including the dialysis room, dressing room, and transportation (6). Based on this background, a sensitive testing screening for the early diagnosis of COVID-19 might be an ideal solution to prevent deadly outbreaks within the dialysis units (7). Unfortunately, no guidelines have been released on the utility of screening for the high-risk HD population until now. COVID-19 screening program is often facultative and modalities vary enormously among HD centers worldwide. Universal screening may be useful in settings with high community prevalence (8). Two types of diagnostic tests are currently used for assessing COVID-19: detection of viral RNA

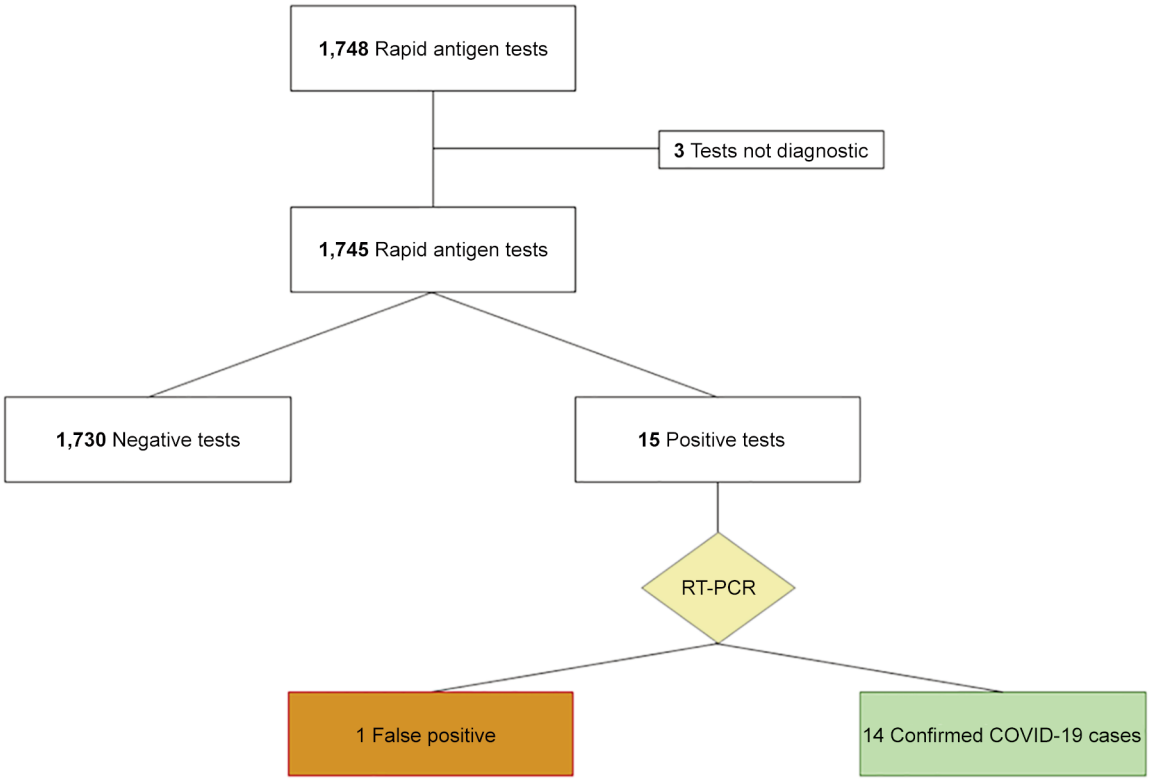

Figure 1. *Flowchart of rapid antigen test screening in patients on in-center hemodialysis.*

through reverse transcription-polymerase chain reaction (RT-PCR) (reference standard) and detection of viral antigens through immunodiagnostic techniques, namely, rapid antigen test (9). As a screening test should place few demands on the healthcare system and be easily accessible and cost-effective, we performed a routine screening based on a weekly rapid antigen test for all asymptomatic HD patients. Thus, our study aimed to describe the performance of a weekly rapid antigen test using nasal swab in the HD population during a period of high virus diffusion.

Patients and Methods

The electronic charts of chronic HD patients who underwent rapid antigen test screening from December 27, 2021 to March 13, 2022, were reviewed retrospectively. A new generation antigen test (LIAISON® SARS-CoV-2 Ag assay) was performed on the anterior nasal swab. It was processed using a chemiluminescence sandwich-immunoassay (CLIA) technology for the quantitative detection of SARS-CoV-2 nucleocapsid antigen protein. This assay reports clinical sensitivity and a clinical specificity of 98.0% and 99.5%, respectively, on nasal samples positive for RT-PCR within 10 days of the onset of symptoms (manufacturer's information).

Rapid antigen test screening was performed every week in all asymptomatic patients as a COVID-19 prevention measure. Before dialysis entry, body temperature, masking, COVID-19 symptoms, and handwashing using alcohol-based hand sanitizer were checked by dialysis nurses. The antigen test was performed as a universal screening in asymptomatic patients through a nasal swab by trained nurses during the dialysis treatment. All antigen-positive tests were confirmed within a few hours through nasopharyngeal swab RT-PCR testing. During the observational period, all patients screened by antigen test underwent nasopharyngeal swab RT-PCR testing (symptom-based screening) principally in case of symptoms (fever, cough, diarrhea, loss of smell and taste, nasal congestion and rhinorrhea, vomit). RT-PCR testing was also performed to monitor the viral shedding of HD patients with COVID-19. Patients who resulted positive from the RT-PCR nasopharyngeal swab were no longer screened by rapid antigen test until two negative RT-PCR nasopharyngeal swab results. Infected patients underwent HD treatment in an isolated room until the resolution of the infection. All health care workers of the University Hospital of Modena received COVID-19 vaccine and were screened through RT-PCR nasopharyngeal swab on request or in case of symptoms.

Ethical Committee approval. The study protocol was approved by the local Ethical Committee (839/2020/OSS/AOUMO).

Statistical analysis. Baseline characteristics were described using mean and standard deviation (SD). The percentage was used to describe categorical variables. Predictive values of the antigen test referred to the percentage of all positive tests that were true positives. Statistical analysis was performed using SPSS 24® (IBM, Armonk, NY, USA) statistical software.

Table I. *Demographic and clinical characteristics of asymptomatic patients who resulted positive to the rapid antigen test screening.*

Case	Sex	Age	Time elapsed from antigen test to RT-PCR (h)	SARS-CoV-2 vaccination	Symptoms	Lung pneumonia	SARS-CoV-2 shedding measured by RT-PCR (day)	Follow-up (day)	Outcome
#1	M	63.4	2.5	Yes	Fever, cough	Yes	33	50.4	Survivor
#2	M	86.1	1.9	Yes	None	No	32.1	79.6	Survivor
#3	M	50.2	2.6	Yes	None	No	25.9	80.6	Survivor
#4	F	51.6	31.0	Yes	Cough	No	23.7	66.6	Survivor
#5	F	41.4	2.0	Yes	None	No	16.8	78.4	Survivor
#6	F	94.6	6.0	Yes	Cough	No	38.8	57.4	Survivor
#7	M	60.8	2.0	Yes	Cough	No	32.9	75.6	Survivor
#8	F	60.2	2.7	Yes	None	No	27.6	50.4	Survivor
#9	M	53.2	5.4	Yes	None	No	25.8	94.4	Survivor
#10	M	79.5	19.6	Yes	Fever, cough, dyspnea	Yes	/	13.4	Deceased
#11	F	76.6	20.1	Yes	Cough	No	38.2	73.6	Survivor
#12	M	89.5	2.3	Yes	None	No	43.9	87.6	Survivor
#13	F	39.0	3.5	Yes	Cough, nasal congestion	No	34.9	21.4	Survivor
#14	F	77.2	3	Yes	None	No	42.3	74.8	Survivor

Results

Over an 11-week period, 1,748 rapid antigen tests were performed in 220 in-center HD patients. On average, rapid antigen test was performed 7.9 times per patient (Figure 1). Patients' mean age was 68.4±14.6 years. A predominance of males (59.5%) was observed in our cohort.

Rapid antigen test yielded a positive result in 15 patients and all but one were confirmed by RT-PCR nasopharyngeal swab after 7.8±9.4 hours (Table I). All COVID-19 patients continued dialysis in our center in a dedicated room. Manifestations of SARS-CoV-2 infection varied between patients. Overall, COVID-19 manifested with no symptoms (n. 7; 50%), mild symptoms (including nasal congestion, cough and sore throat) (n. 4; 28%), lung pneumonia (n. 2; 14.2%), and severe illness with a poor outcome (n.1; 7.1%). In the survivors, nasal viral shedding measured by the means of RT-PCR continued for 31.9±7.8 days from the diagnosis of COVID-19. Follow-up of these patients lasted 63.8±25.4 days from the diagnosis of COVID-19.

Overall, testing screening with rapid antigen test detected 14 out of 26 (53.8%) COVID-19 cases during the study period. Considering the RT-PCR test as the reference standard for the diagnosis of SARS-CoV-2 infection, the positive predicted value (PPV) of the rapid antigen test accounted for 93%.

During the study period, 12 symptomatic patients who underwent regular rapid antigen test screening were diagnosed with COVID-19 by RT-PCR nasopharyngeal swab. In these patients, the molecular assay was performed after 4.7±2.3 days from the negative result of the rapid antigen test.

Discussion

This study reports the results of a rapid antigen test screening for SARS-CoV-2 infection in a large HD population. Rapid antigen test screening, performed once a week on asymptomatic patients, identified 53.8% of the COVID-19 cases during the fourth COVID-19 wave in Italy, driven principally by the spread of Delta and Omicron variants (10). The utility of this screening program has been substantial because patients with a new COVID-19 diagnosis have been timely grouped with other infected patients. Considering about half of the patients diagnosed with COVID-19 remained asymptomatic throughout the course of infection, the screening program has identified infected patients who would never develop clear symptoms of COVID-19. In this way, early detection of SARS-CoV-2 infection has played an important role in the implementation of containment interventions against SARS-CoV-2 diffusion among frail patients. These measures have been critical to isolate asymptomatic with COVID-19 from healthy patients. It is well known that asymptomatic patients may contribute to disease spread among HD patients, as transmission from asymptomatic individuals has been estimated to account for more than half of all cases of COVID-19 (11).

The findings of our studies also underline that the antigen test screening was unable to detect all COVID-19 cases in our population, although it was carried out once a week. Twelve patients with negative antigen screening developed symptoms of COVID-19 on average 4.7±2.3 days later.

Taken together, these data seem to underestimate the overall COVID-19 testing capacity of the rapid antigen test. Although rapid antigen test has a slightly lower diagnostic power in terms of sensitivity and specificity than RT-PCR, we believe that the concerns about the underdiagnosis of COVID-19 cases may be attributed to the virus dynamics rather than to the performance of the antigen test. The short incubation period of the new SARS-CoV-2 variants (on average 3.2 days for Omicron variant and 4.4 days for other variants) might have undermined the performance of the antigen test (12). Based on these data, the question that arises is whether weekly rapid antigen test screening is a useful preventive measure in HD patients. We considered the performance of the rapid antigen test good, as the predictive positive predictive value of the antigen test accounted for 93%. Rapid antigen test using nasal swab has the advantage over RT-PCR nasopharyngeal swab to be less invasive, less time-consuming, and physically less discomforting for the patients. Antigen diagnostic tests make the screening program efficient and effective in the HD unit, as test results are obtained in a few hours and always before the next dialysis session (13, 14). Lastly, this test can be also a convenient solution in situations in which RT-PCR testing capacity is limited given its better cost profile (average cost of $5.4 *vs.* $19.6 per test in our hospital). On the other hand, the shorter incubation period of the last variants of SARS-CoV-2 infection emphasizes the need for more frequent testing, especially during a time of high community prevalence of the virus (13). For instance, twice-weekly rapid testing might be a solution to overcome the short period of incubation of the newer variants. This hypothesis, theoretically conceivable, should consider local human and financial resources, space for isolation, as well as laboratory workload in the setting of the COVID-19 pandemic. However, a great deal of attention is then required for the potential of rapid antigen tests to determine false-positives results (15). Given the risk of grouping uninfected patients with COVID-19 subjects, we believe that confirmatory RT-PCR information is still crucial in this setting.

Some limitations should be enunciated. First, the study was not designed to express the sensitivity, specificity, and adequacy of the screening test. Therefore, the evaluation of the analytical performance of the rapid antigen test is beyond the aim of this study. Second, we cannot establish the incubation time of the illness as virus variants have not been detected during the observational study. Third, we are unaware of the performance of the rapid antigen test in HD patients, a small subset of the population with multiple comorbidities. Lastly, we do not know the source of SARS-CoV-2 infection in our patients, even though we suppose it spread within households in most cases.

In conclusion, weekly rapid antigen test screening for COVID-19 in patients on in-center HD is a useful preventive measure to further reduce virus transmission through early detection of COVID-19 cases. However, the short period of incubation of the new SARS-CoV-2 variants should be considered for future screening programs using rapid antigen test.

Conflicts of Interest

The Authors have no conflicts of interest to declare in relation to this study.

Authors' Contributions

GA: Conceptualization; RS, AM, SG, GL: Data curation, Writing-original draft preparation; FF: Writing-reviewing and editing; MP, WG: Investigation; MG, GG, GC, GD, RM: reviewed the manuscript.

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