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De-isolation of vaccinated COVID-19 health care workers using rapid antigen detection test



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ABSTRACT

Background: COVID-19 de-isolation guidelines of health care workers (HCW) were formulated based on evidence describing the duration of infectious viral shedding of the wild SARS-CoV-2 virus. During the periods of COVID-19 vaccination and variants, a test-based approach was recommended to end isolation of HCW, based on emerging data describing the viral kinetics of COVID-19 variants. While Rapid antigen detection tests (RADT) are increasingly used in the diagnosis of COVID-19, their use is limited in de-isolation.

Methods: We described the use of RADT in the de-isolation of COVID-19 vaccinated HCW with mild infection who were asymptomatic on day 7 post diagnosis in a single center retrospective cohort study during the Omicron surge.

Results: Of the 480 HCWs, 173 (36%) had positive RADT. The positivity rate of RADT was not different in HCW who received two doses versus three doses of vaccine (34.4% versus 40.3%, $p = 0.239$).

Conclusions: A symptom based, test-based approach using RADT is a useful tool in the de-isolation of HCW, with mild disease, in the era of Omicron. Further studies are required to evaluate the role of RADT in de-isolation of patients with severe COVID-19 disease.

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1. Introduction

The emergence of Omicron variant worldwide was associated with a surge in the number of COVID-19 cases in the community and hospital outbreaks [1]. Understanding SARS-CoV-2 viral kinetics of

variants is crucial to develop appropriate infection preventive protocols for COVID-19 [2]. Studies describing the viral kinetics of the wild SARS-CoV-2 showed that the risk of infectious viral shedding and risk of viral transmission is 8 days post symptoms onset [3]. During the Delta variant period, one study described that positive viral cultures were detected for 7 days post symptoms onset in a cohort of vaccinated COVID-19 patients [4], while another study showed that the duration of replication competent virus was 5 days versus 10 days in a cohort of vaccinated and unvaccinated COVID-19 patients respectively [5]. A recent study showed that the time to

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viral conversion was 6 days post symptoms onset and it was not different between COVID-19 vaccinated patients infected with Delta and Omicron variants [6]. In another study, during the Omicron Era, the duration of infectious viral shedding was up to 8 days post symptoms onset among a cohort of COVID-19 vaccinated patients. None of the patients had a positive viral culture at day 10 post symptoms onset and most patients had a negative viral culture at day 5 post symptoms onset [7]. Currently, international guidelines for de-isolation of health care workers (HCWs) are recommending a test-based approach at day 7 post symptoms onset [8,9]. Rapid antigen detection tests (RADT) are increasingly used in COVID-19 diagnosis with reliable sensitivity, acceptable specificity, and short turn-around time. They are cheap and do not require an experienced laboratory personnel [10]. There is limited data on the use RADT on de-isolation of HCWs. Thus, we evaluated the performance of RADT on vaccinated HCWs infected with SARS-CoV-2 according to the Saudi Arabian ministry of health guidelines in the era of Omicron variant, which were comparable to the American and European guidelines [11].

2. Methods

2.1. Study participants and de-isolation protocol

A single center, retrospective cohort study was conducted among all HCWs diagnosed with COVID-19 based on positive SARS-CoV-2 PCR, between 11th January and 12th February. All home isolated HCWs with mild disease (upper respiratory tract infection) were included, while those requiring hospitalization were excluded.

At day 7 post diagnosis, HCWs were called by infection control practitioners to assess resolution of symptoms and eligibility to perform RADT for de-isolation. A nasal swab for RADT was performed for asymptomatic HCWs by a trained nurse in the HCW de-isolation clinic. HCWs with negative RADT were declared recovered and were eligible to return to work. On the other hands, HCWs with positive RADT were isolated for 10 days without repeating the test. In addition, HCW who were symptomatic on day 7 post diagnosis were isolated for 10 days without performing RADT.

Omicron was the predominant SARS-CoV-2 circulating variant during the study period based on our hospital surveillance next generation genome sequencing of COVID-19 which showed 780 out of 808 (96.5%) of cases were classified as B.1.1.529 Omicron variants (Alhamlan FS et al. unpublished data).

The work was one of the projects of the Department of Infection Control and Hospital Epidemiology during COVID-19 Omicron pandemic.

2.2. RADT description

Panbio™ COVID-19 Antigen rapid test (Abbott, USA) was performed following the manufacturer's instructions, within 15 min from the time of nasal swab collection [12]. Briefly, the presence of the test line (T) and the control line (C) within the result window, regardless of which line appears first, indicates a positive result. The presence of only the control line (C) and no test line (T) within the result window.

indicates a negative result. If the control line (C) is not visible within the result window after performing the test, the result is considered invalid.

2.3. Statistical analysis

Electronic charts were reviewed for demographics, vaccination status, disease severity and duration between last vaccine dose and breakthrough infections. Chi-square test or Fisher's exact test were used to compare categorical variables. T-test or Mann-Whitney test

Table 1

Demographics and vaccination status of HCW in relation to the results of RADT at day 7 post diagnosis.

	Total	Positive	Negative	p-value
Age				
Mean ± SD	37.5 ± 8.7	37.5 ± 8.7	37.6 ± 8.8	0.878
< 35	193 (40.4%)	71 (36.8%)	122 (63.2%)	0.948
35–44	182 (38.1%)	64 (35.2%)	118 (64.8%)	
≥ 45	103 (21.5%)	37 (35.9%)	66 (64.1%)	
Gender				
Male	176 (36.7%)	69 (39.2%)	107 (60.8%)	0.252
Female	303 (63.3%)	103 (34.0%)	200 (66.0%)	
Profession				
Nurse	192 (40.0%)	59 (30.7%)	133 (69.3%)	0.048
Physician	75 (15.6%)	33 (44.0%)	42 (56.0%)	0.118
Others	213 (44.4%)	81 (38.0%)	132 (62.0%)	0.418
Unit				
ICU	36 (7.5%)	11 (30.6%)	25 (69.4%)	0.476
ER	54 (11.3%)	21 (38.9%)	33 (61.1%)	0.644
Laboratory/ radiology/ pharmacy	67 (14.0%)	30 (44.8%)	37 (55.2%)	0.108
Respiratory therapy	18 (3.8%)	7 (38.9%)	11 (61.1%)	0.798
OR	25 (5.2%)	6 (24.0%)	19 (76.0%)	0.198
Wards	178 (37.1%)	63 (35.4%)	115 (64.6%)	0.820
Outpatient	50 (10.4%)	17 (34.0%)	33 (66.0%)	0.751
Non-clinical	52 (10.8%)	18 (34.6%)	34 (65.4%)	0.821
Vaccination status				
Two doses	358 (75.1%)	123 (34.4%)	235 (65.6%)	0.239
Three doses	119 (24.9%)	48 (40.3%)	71 (59.7%)	
Duration in days related to vaccine (mean SD)				
Between dose 1 and dose 2	98.2 ± 46.4	93.9 ± 45.7	100.6 ± 46.7	0.353
Between dose 2 and dose 3	200.0 ± 54.2	203.8 ± 60.3	197.6 ± 50.1	0.474
Between dose 1 and dose 3	293.9 ± 40.4	295.5 ± 42.5	292.8 ± 39.2	0.537
Duration in days between last vaccine dose and COVID-19 infection (mean SD)	52.5 ± 78.8	48.8 ± 79.8	54.6 ± 78.4	0.298

were used to compare continuous variables. Statistical Package for the Social Sciences software (SPSS Version 27.0. Armonk, NY: IBM Corp) were utilized.

3. Results

A total of 480 HCWs with mild COVID-19 were included in the study with a mean age of 37.5 ± 8.7 years. 303 (63%) were females, 192 (40%) were nurses and 75 (16%) were physicians. 358 (75.1%) and 119 (24.9%) had received two and three doses of COVID-19 vaccine respectively. The duration between the last vaccine dose and breakthrough COVID-19 infection was 52 days (SD 78.8). 173/480 (36%) had positive RADT on day 7 post diagnosis.

A total 123 out of 358 (34.4%) HCW vaccinated with two doses had positive RADT, while 48 out of 119 (40.3%) HCW vaccinated with three doses had positive RADT (p = 0.239). (Table 1).

4. Discussion

We described the performance of RADT in de-isolation of 480 vaccinated COVID-19 HCW in the era of Omicron variant at day 7 post diagnosis. Almost one third of the asymptomatic HCWs had

positive RADT and their isolation was extended to 10 days. The positivity of RADT was not different between HCW who received two versus three doses of COVID-19 vaccine.

Several studies evaluated the performance of different RADT compared to RT-PCR and viral cultures [6,13–15]. A study of 206 COVID-19 samples compared the sensitivity and specificity of 4 different RADT to SARS-CoV-2 viral cultures. The sensitivities were 90%, 74%, 74%, 74% and the specificities were 70%, 92%, 91%, 92% for Lumira, BD veritor, Carestart and Oscar respectively [13]. Another study compared the performance of Aboott panbio (the same RADT used in our study) to RT-PCR among 4183 patients with non-severe COVID-19. The overall sensitivity, specificity, positive predictive value and negative predictive value for the RADT was 82.1%, 99.1%, 95.3% and 96.3% respectively. The sensitivity of the RADT test improved to 89.3% when evaluating patients with symptoms onset less than 7 days and RT-PCR Ct values less than 24 [14]. A recent study compared the performance of RADT to viral culture among a cohort of 19 and 37 cases of Omicron and Delta. The overall RADT sensitivity and specificity was 72% and 85% respectively. Based on symptoms onset, the sensitivity of RADT was 81% and 50% while the specificity was 67% and 88% respectively for patients with symptoms onset less than 5 days and symptoms onset 6–10 days. Based on the COVID-19 variant, the sensitivity of RADT was 78% and 69%, while the specificity was 84% and 85% among Omicron and Delta cases respectively [6]. Although RADT are lacking sensitivity compared to RT-PCR, compared to viral culture, RADT had 96.2% sensitivity and 91% specificity with good concordance and thus they are useful diagnostic tools to predict that COVID-19 individuals are contagious [15].

Our results were comparable to the findings of a study which showed a decline in the positivity rate of RADT among 260 HCWs from 46% to 38% on day 5 and day 7 post symptom onset [16]. In addition, both studies showed that a booster vaccine dose was not associated with a shorter duration of RADT viral shedding compared to two doses. A recent study evaluated the role of RADT in the de-isolation of 729 patients in USA, half of them were unvaccinated [17]. On day 9, 38% had a positive RADT regardless of symptoms, while on day 7, The positivity of RADT was 66% and 3% in symptomatic and asymptomatic patients respectively. The main limitation of de-isolation studies was the challenge of performing viral cultures. In addition, our study was limited by the lack of serial RADT.

A recent study described the impact of two doses and a booster third dose vaccination on RNA genomic copies and infectious viral load shedding in a cohort of patients infected with Omicron variants. In addition, RNA genomic copies and infectious viral load clearance was compared between two doses vaccinated and unvaccinated patients infected with Delta variants. In patients infected with Delta variants, two doses vaccination reduced infectious viral load shedding but did not affect the RNA genomic copies clearance over 5 days post symptoms onset. On the other hands, in patients infected with Omicron variants, the two doses vaccination did not reduce RNA and infectious viral shedding. Interestingly, a third booster dose vaccine reduced infectious viral load shedding but did not affect the RNA genomic copies clearance over 5 days post symptoms onset in patients infected with Omicron variants. RADT were not performed in this study and the impact of booster vaccination on results of RADT could not be evaluated [2].

In the presence of circulating SARS-CoV-2 variants, although RADT are lacking diagnostic sensitivity in asymptomatic individuals, they could be a suitable test for ending isolation as they are identifying the infectious phase of COVID-19 unlike nucleic acid amplification tests which remained positive beyond this phase [18]. WHO recommended the use of RADT with 80% sensitivity and 97% specificity compared to RT-PCR. The application of RADT in public health setting is useful to exclude individuals that are infectious and pose a risk of COVID-19 transmission in communities and hospitals [3].

Future studies are needed to evaluate the role of RADT in de-isolation of COVID-19 patients with severe disease and immunosuppression.

5. Conclusions

Among a cohort of vaccinated HCW with mild COVID-19 disease during the Omicron surge, a symptom and a RADT based approach was adopted at day 7 to allow HCW to return to work. One third of vaccinated HCW had positive RADT at day 7 post diagnosis and extended their isolation to 10 days. The use of RADT at day 7 post diagnosis is a promising tool to end the isolation of asymptomatic and vaccinated HCW with COVID-19 in the era of Omicron. This approach is effective to avoid staff shortage and prevent nosocomial transmission of SARS-CoV-2 infection. With the emergence of other SARS-CoV-2 variants, future studies are needed to evaluate the performance of RADT at day 7 and day 10 post diagnosis.

CRedit authorship contribution statement

All authors contributed equally to this research; Study concept, Data acquisition, Data analysis, Performing the experiment, Writing and reviewing the manuscript.

Ethical approval

This reserach was approved by the institutional research board, King Faisal Specialist Hospital and Research Centre, Jeddah, Saudi Arabia.

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Conflict of interest

None.

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