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ORIGINAL PAPER

Comparison of a novel antigen detection test with reverse transcription polymerase chain reaction assay for laboratory diagnosis of SARS-CoV-2 infection

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Abstract

Molecular diagnosis of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by real-time reverse transcription polymerase chain reaction (RT-PCR) in respiratory specimens is considered the gold standard method. This method is highly sensitive and specific but it has some limitations such as being expensive and requiring special laboratory equipment and skilled personnel. RapidFor™ Antigen Rapid Test Kit is a commercially available Ag-RDT which is produced in Turkey and designed to detect the nucleocapsid antigen of SARS-CoV-2 in nasopharyngeal swab samples. The aim of this study was to evaluate the performance of this novel SARS-CoV-2 antigen detection considering the RT-PCR method as the gold standard. Four hundred forty-four nasopharyngeal swab samples which were collected from the patients who met clinical criteria of COVID-19 from ten centers in Turkey between September 2020 and February 2021 were included in the study. All the nasopharyngeal swab samples were tested for SARS-CoV-2 RNA using commercial RT-PCR kits (Bioeksen and A1 Lifesciences, İstanbul, Turkey) according to the manufacturer's instructions. Viral loads were assessed according to the cycle threshold (Ct) values. RapidFor™ SARS-CoV-2 antigen test (Vitrosens Biotechnology, Istanbul, Turkey) was used to investigate the presence of SARS-CoV-2 antigen in all samples following the manufacturer's instructions. Out of 444 nasopharyngeal swab samples tested, 346 (77.9%) were positive and 98 (22.1%) were negative for SARS-CoV-2 RNA by RTPCR. Overall sensitivity of the RapidFor™. Antigen Rapid Test Kit was 80.3% whereas specificity was found to be 87.8%. Positivity rate of rapid antigen test in samples with Ct values over 25 and below 30 was 82.7%, while it increased to 95.7% in samples $20 \leq Ct < 25$ and reached 100% in samples with Ct values below 20. RapidFor™ SARS-CoV-2 Ag test might be a good choice in the screening of symptomatic and asymptomatic patients and their contacts for taking isolation measures early, with advantages over RT-PCR as being rapid, easy and being applicable in every laboratory and even at point of care.

Keywords COVID-19 · Nasopharyngeal swab samples · Rapid antigen test · RT-PCR · SARS-CoV-2

Introduction

Molecular diagnosis of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by real-time reverse transcription polymerase chain reaction (RT-PCR) in respiratory specimens is considered gold standard method [1, 2]. This method is highly sensitive and specific, but it has some limitations such as being expensive and requiring special laboratory equipments and skilled personnel. Although it is normally possible to get results in less than 2 h, most test results are usually delayed because of the huge number of samples sent to molecular diagnostic laboratories, during pandemics. This is important as it causes people wait for the result and leads to a delay in isolation of patients who are

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found to be positive. Therefore, it is certain that rapid and easy laboratory tests which give accurate results are needed to control the spread of the virus.

Antigen-detection rapid diagnostic tests (Ag-RDTs) are immunochromatic tests which are used to detect SARS-CoV-2 antigen. They are known as less sensitive than SARS-CoV-2 RT-PCR method, but seem advantageous as they do not have the requirement of special laboratory facilities and skilled personnel. They are easy to perform, cheap and it is possible to get rapid results. Some of these tests are approved by Food and Drug Administration FDA and is used as first-line diagnostic tests in Belgium [3, 4].

RapidFor™ Antigen Rapid Test Kit is a commercially available Ag-RDT which is produced in Turkey and designed to detect the nucleocapsid antigen of SARS-CoV-2 in nasopharyngeal swab samples (NPS). Since the test determines the nucleocapsid antigen it is expected to detect the variants of the virus that emerge due to mutations seen in the genes of spike antigen. The aim of this study was to evaluate the performance of this novel SARS-CoV-2 antigen detection considering the RT-PCR method as gold standard.

Patients and methods

Four hundred and forty-four NPS which were collected from randomly selected patients over age of 13 who met clinical criteria of COVID-19 from 10 centers located in seven cities in six different regions between September 2020 and February 2021 were included in the study, for representing general population in Turkey. The median age of the patients was 49 (13–92), while 229 (51.9%) were females. All the patients enrolled to the study acknowledged understanding the aims of the study and signed an informed consent prior to collection of clinical samples.

NPS were sent to laboratory in viral nucleic acid transport medium (VNAT). Among 444 samples, 237 (53,4%) were tested by RT-PCR and antigen testing soon after arrival to the laboratory, while 207 (46,6%) were frozen and stored to be tested later due to the laboratories' working capacity.

All NPS were tested for SARS-CoV-2 RNA using commercial RT-PCR kits (Bioeksen and A1 Lifesciences, İstanbul, Turkey) according to the manufacturer's instructions. Viral loads were assessed according to the cycle threshold (Ct) values.

RapidFor™ SARS-CoV-2 antigen test (Vitrosens Biotechnology, Istanbul, Turkey) was used to investigate the presence of SARS-CoV-2 antigen in all samples following the manufacturer's instructions. Briefly, 500µL sample buffer was added to a tube. The swab was completely immersed in the tube and rotated 10 times. The swab was discarded after squeezing along the inner wall of the tube. 100µL (3 drops) of processed samples were added to the sample well. After 15 min the results were read visually. Test cards which showed both control (C) and test (T) lines were considered positive.

Statistical analysis

Categorical data were presented in numbers and percentages and continuous data were presented as mean, median and range. Statistical analyses was performed using a statistical software, IBM SPSS Statistics (version 23). SARS-CoV-2 RT-PCR was considered as the gold standard method and Cohen's kappa coefficient (κ) was used to evaluate the agreement between tests. p value less than or equal to 0.05 was considered significant.

Results

A total of 444 NPS samples were studied. The median age of the patients was 49 (13–92), while 229 (51.9%) were females. Among the 444 samples, 53.4% were tested directly after arrival to the laboratory, while 46.6% were frozen and stored before testing.

Out of 444 nasopharyngeal swab samples tested, 346 (77.9%) were positive and 98 (22.1%) were negative for SARS-CoV-2 RNA by RT-PCR. Median Ct value of SARS-CoV-2 PCR positive NPS samples was 25.15 (mean;35.42; range: 11.96–42.19). Two hundred and ninety (65.3%) of all NPS samples were positive by rapid antigen test while 154 (34.7%) were negative.

Overall sensitivity of the RapidFor TM Antigen Rapid Test Kit was 80.3%, whereas specificity was found to be 87.8%. Agreement of this Ag-RDT with PCR was found moderate ($\kappa = 0.565$, $p < 0.001$). Median Ct value of the Ag-RDT positive samples was 23.67 (mean: 23.81; range: 11.96–37.20). Out of 98 RT-PCR negative samples, 12 (12.2%) were positive by the rapid antigen test.

Positivity rate of rapid antigen test in samples with Ct values over 25 and below 30 was 82.7%, while it increased to 95.7% in samples $20 \leq Ct < 25$ and reached 100% in samples with Ct values below 20. Out of RT-PCR positive 92 samples with Ct values between 20 and 25, 4 samples (4.3%) were negative by rapid antigen test. Detailed comparison of NPS Ag-RDT results according to the Ct values of NPS RT-PCR test is given in Table 1.

Rapid antigen test positivity rates of RT-PCR positive NPS differed amongst the centers, ranging from 40% to 97.1%.

Positivity rates according to age groups and gender are shown in Table 2. One hundred twenty five out of 207 (60.4%) frozen NPS samples were positive by Ag-RDT while 165 of 237 (69.6%) fresh NPS samples gave positive result.

Table 1 Comparison of NPS Ag-RDT results according to the Ct values of NPS RT-PCR test

Ct value	Antigen test number	NPS RT-PCR positive									
		Antigen positive					Antigen negative				
		n	%	Median Ct	Lowest Ct	Highest Ct	*n*	%	Median Ct	Lowest Ct	Highest Ct
Ct < 20	74	74	100	18.36	11.96	19.96	–	–	–	–	–
20 ≤ Ct < 25	92	88	95.7	22.37	20	24.99	4	4.3	23.19	21.47	24.07
25 ≤ Ct < 30	104	86	82.7	27.26	25	25.99	18	17.3	28.16	25.66	29.90
30 ≤ Ct < 35	52	25	48.1	31.93	30	34.57	27	51.9	31	30	34.91
Ct ≥ 35	24	5	20.8	36.50	35.31	37.20	19	79.2	37.96	35	42.19
Total	346	278	80.3	23.67	11.96	37.20	68	19.7	30.74	21.47	42.1
		NPS RT-PCR negative									
		Antigen positive					Antigen negative				
PCR negative	98	12	12.2	–	–	–	86	87.8	–	–	–

Table 2 Positivity rates according to age groups and gender

	Antigen positive		Antigen negative	
	n	%	*n*	%
Age groups				
13–25	40	64.5	22	35.5
26–40	61	61	39	39
41–60	85	69.1	38	30.9
≥ 61	99	70,2	42	11.5
Gender				
Female	149	65.1	80	34.9
Male	140	66.0	72	34

Discussion

In this study, we evaluated the performance of an Ag-RDT, RapidFor™ in comparison to RT-PCR method for detection of SARS-CoV-2 in nasopharyngeal swab samples. To the best of our knowledge, this is the first multicenter study evaluating the performance of a rapid antigen test which is produced in Turkey.

Considering the laboratory diagnosis of SARS-CoV2 infection, needs of molecular diagnostics laboratories such as expensive and special equipment, skilled personnel and disadvantages like long turnaround times and high workload of the laboratory, led to development of various Ag-RDTs which are inexpensive and easy to use. Many studies were conducted to evaluate these tests and reported variable performances for them [3, 5–12].

Some studies reported very low sensitivities and suggested that use of these tests was not suitable in clinical settings because of the false negative results [3, 7]. In one of these studies, the Coris COVID-19 Ag Respi-Strip test was reported to have a low (30.2%) overall sensitivity, but it achieved a high sensitivity (100%) for the samples with Ct values under 25. In this study, median Ct of the 74 discordant samples (positive RT-qPCR with negative rapid test) was 35 (25–38) [3].

In another study, two Ag-RDTs (detecting SARS-CoV-2 nucleoprotein antigens), Panbio and SD-Biosensor, were proven to have excellent agreement for samples with high viral loads and for samples which were obtained within 7 days after the onset of the disease [6]. In this study, 186 RT-PCR negative and 170 RT-PCR positive samples were included to test the sensitivity and specificity of these tests. Although overall sensitivities of Panbio and SD-Biosensor were 60.0% and 66.5%, respectively, both tests had highest sensitivity (100%) for the samples of which viral loads were high with Ct values under 20. The specificities of the two tests were high [6]. They were reported to be100% for Panbio and 97.3% for SD-Biosensor.

Common conclusion of many studies was that Ag-RDTs showed higher sensitivity especially in samples which 6.

853had high viral loads [3, 6, 9, 10, 13] and within the first days of onset of the disease [6, 9, 12, 14]. Some Ag-RDTs were even recommended to be used as a first line diagnostic tool in some countries [2, 3, 15–17]. In one study, an Ag-RDT, Panbio COVID-19 was tested as a point-of-care testing (POCT) method in primary healthcare centers. Overall sensitivity and specificity of the test was found as 79.6% and 100%, respectively, suggesting it as a good point-of-care testing (POC) tool [14].

Previously, it had been shown that higher viral loads in nasopharyngeal swab samples were associated with higher risk of transmission and developing symptomatic COVID-19 with shorter incubation periods [18]. In addition, viral loads of the patients were shown to be high especially within the 3 days before the onset of the symptoms and 5–7 days after the symptoms appear [19–21]. Therefore, it is important to determine patients with high viral loads as early as possible in order to take isolation

precautions. As these tests are inexpensive and easy to use, frequent screening of asymptomatic and symptomatic patients and people in contact with these patients might give the advantage of detecting patients in their short incubation periods before having symptoms. In our study, information of sample timing is lacking for many of the centers, therefore we couldn't examine the positivity rates according to the days of sample collection.

On the other hand, the correlation between Ct values and infectivity was not proven. It was shown that virus could still be cultured in specimens with Ct values over 30 [20, 22] or after 10th day of the onset of the symptoms [23]. According to these studies, there might not be any correlation between Ct values and infectivity.

According to the data obtained in Germany where Ag-RDTs were used widely in diagnosis of SARS-CoV2 infection, one of the main disadvantages of Ag-RDTs was reported as false positives (Kretschmer A). It was suggested that false positive results might have led to high economic burden and unnecessary isolation precautions. Considering that prevalence of SARS-CoV2 infection changes at different times and regions, relying on only Ag-RDT when the prevalence is low might not be safe.

Our results were comparable to the results of other studies. Overall sensitivity of our test was 80.3% and fulfilled the criteria reported by WHO (Ag-2). Sensitivities increased with the higher viral loads, reaching 95.7% and 100% in samples with Ct values between 20–25 and under 20, respectively.

In our study, positivity rates showed differences in centers (40–97.1%). We think that overall sensitivity was affected by the heterogeneous distribution of the samples with different viral loads in different centers. In the center with the lowest sensitivity rate, Ct values of the 91% of samples were above 25. Efficiency of nasopharyngeal swab collection, transport medium used, storage or directly testing of the sample might have been the other factors responsible from different sensitivities in centers. Sample collection might not have been efficient enough in some centers as it was performed in different conditions like emergency departments, several clinics or outpatient clinics. In centers which reported sensitivities over 80%, most samples were tested directly but the center with highest sensitivity had 52.3% of samples with Ct values above 25, but samples were tested directly in this center. In two centers with lowest sensitivities, samples were mostly frozen and stored (91.5% and 99.3%, respectively). This may indicate that testing the sample freshly maybe more effective than testing frozen samples although the percentages of detection of SARS-CoV antigen were 60.4% and 69.6% in frozen and fresh samples respectively, we didn't find statistically difference between frozen and fresh samples collected from all centers".

Processing of samples might have also affected the sensitivity of the Ag-RDT result. One Ag-RDT, Standard Q COVID-19 Antigen kit was found to have very high sensitivity and specificity rates which were 98.33 and 98.73, respectively [5]. In this study, for highly viscous samples, more VTM were added to reduce the viscosity and vortexed using glass beads to disrupt the thick mucus before testing. Scohy et al. [3] tried ultracentrifugation of the samples with discordant results (RT-PCR positive, Ag-RDT negative), only two of 24 samples became weakly positive. We did not perform any additional procedures for viscous samples or samples with discordant results.

Although the Ag-RDTs have good sensitivity in laboratory conditions, it was shown that sensitivity was lower under field conditions [24]. Similar field study for RapidFor™ Ag-RDT will be beneficial.

Our study presents some limitations. As the 46.6% percentage of the samples were frozen and stored before testing, studying of frozen samples might have led to degradation of the antigen. Manufacturer of the kit recommended that samples should be tested freshly, but in our study, workload in some centers did not allow to test the samples immediately. Another limitation is that processing of samples before testing had some differences in centers. Samples were transported to the laboratory in viral transport medium. Some centers tested the samples transported in VNAT directly without using buffer provided in the kit while some added buffer to the sample before testing. We assume that testing the sample directly without using any viral transport medium as a POC test might improve the sensitivity. According to these, new prospective studies with larger sample cases are needed. Another limitation of our study is that we do not have the information about timing of taking samples from patients for most of the centers and we did not classify the patients according to their signs and symptoms.

RapidFor™ Ag-RDT proved to be a useful, inexpensive and easy test showing a sensitivity of 100% in samples with high viral loads which have a Ct value lower than 20 by RT-PCR and a comparable sensitivity for samples with Ct values up to 30 by RT-PCR. It might play an important role in breaking the chain of transmission by rapid identification and isolation of Covid19 patients with high loads of virus in their respiratory system.

According to WHO, the sensitivity of the Ag-RDTs should be 80% and specificity should be minimum 97% [16, 25]. Sensitivity of RapidForTM SARS-CoV-2 Ag Test meets these criteria.

Conclusions

RapidFor™ SARS-CoV-2 Ag Test might be a good choice in screening of symptomatic and asymptomatic patients and their contacts for taking isolation measures early, especially when the prevalence is high, with advantages as being rapid, easy and applicable in every laboratory and even at point of care.

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Declarations

Conflict of interest No conflict of interest is declared by the authors.

Ethics approval This study has been approved by the Acibadem University Ethics Committee, ATADEK-2020/14.

References

1. Corman VM, Landt O, Kaiser M, Molenkamp R, Meijer A, Chu DK, Bleicker T, Brunink S, Schneider J, Schmidt ML, Mulders DG, Haagmans BL, van der Veer B, van den Brink S, Wijsman L, Goderski G, Romette JL, Ellis J, Zambon M, Peiris M, Goossens H, Reusken C, Koopmans MP, Drosten C. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Euro Surveill. 2020. https://doi.org/10.2807/1560-7917.ES.2020.25.3.2000045.
2. OMS, Laboratory Testing Strategy Recommendations for COVID-19. Interim Guidance, 21 march 2020.
3. Scohy A, Anantharajah A, Bodeus M, Kabamba-Mukadi B, Verroken A, Rodriguez-Villalobos H. Low performance of rapid antigen detection test as frontline testing for COVID-19 diagnosis. J Clin Virol. 2020;129: 104455.
4. Blairon L, Wilmet A, Beukinga I, Tre-Hardy M. Implementation of rapid SARS-CoV-2 antigenic testing in a laboratory without access to molecular methods: experiences of a general hospital. J Clin Virol. 2020;129: 104472.
5. Chaimayo C, Kaewnaphan B, Tanlieng N, Athipanyasilp N, Sirijatuphat R, Chayakulkeeree M, Angkasekwinai N, Sutthent R, Puangpunngam N, Tharmviboonsri T, Pongraweewan O, Chuthapisith S, Sirivatanauksorn Y, Kantakamalakul W, Horthongkham N. Rapid SARS-CoV-2 antigen detection assay in comparison with real-time RT-PCR assay for laboratory diagnosis of COVID-19 in Thailand. Virol J. 2020;17:177.
6. Perez-Garcia F, Romanyk J, Moya Gutierrez H, Labrador Ballestero A, Perez Ranz I, Gonzalez Arroyo J, Gonzalez Ventosa V, Perez-Tanoira R, Domingo Cruz C, Cuadros-Gonzalez J. Comparative evaluation of Panbio and SD biosensor antigen rapid diagnostic tests for COVID-19 diagnosis. J Med Virol. 2021;93:5650–4.
7. Mak GC, Cheng PK, Lau SS, Wong KK, Lau CS, Lam ET, Chan RC, Tsang DN. Evaluation of rapid antigen test for detection of SARS-CoV-2 virus. J Clin Virol. 2020;129: 104500.
8. Perez-Garcia F, Perez-Tanoira R, Romanyk J, Arroyo T, Gomez-Herruz P, Cuadros-Gonzalez J. Alltest rapid lateral flow immunoassays is reliable in diagnosing SARS-CoV-2 infection from 14 days after symptom onset: a prospective single-center study. J Clin Virol. 2020;129: 104473.
9. Aoki K, Nagasawa T, Ishii Y, Yagi S, Kashiwagi K, Miyazaki T, Tateda K. Evaluation of clinical utility of novel coronavirus antigen detection reagent, Espline(R) SARS-CoV-2. J Infect Chemother. 2021;27:319–22.
10. Ishii T, Sasaki M, Yamada K, Kato D, Osuka H, Aoki K, Morita T, Ishii Y, Tateda K. Immunochromatography and chemiluminescent enzyme immunoassay for COVID-19 diagnosis. J Infect Chemother. 2021;27:915–8.
11. Ristic M, Nikolic N, Cabarkapa V, Turkulov V, Petrovic V. Validation of the STANDARD Q COVID-19 antigen test in Vojvodina Serbia. PLoS ONE. 2021;16: e0247606.
12. Linares M, Perez-Tanoira R, Carrero A, Romanyk J, Perez-Garcia F, Gomez-Herruz P, Arroyo T, Cuadros J. Panbio antigen rapid test is reliable to diagnose SARS-CoV-2 infection in the first 7 days after the onset of symptoms. J Clin Virol. 2020;133: 104659.
13. Yamayoshi S, Sakai-Tagawa Y, Koga M, Akasaka O, Nakachi I, Koh H, Maeda K, Adachi E, Saito M, Nagai H, Ikeuchi K, Ogura T, Baba R, Fujita K, Fukui T, Ito F, Hattori SI, Yamamoto K, Nakamoto T, Furusawa Y, Yasuhara A, Ujie M, Yamada S, Ito M, Mitsuya H, Omagari N, Yotsuyanagi H, Iwatsuki-Horimoto K, Imai M, Kawaoka Y. Comparison of rapid antigen tests for COVID-19. Viruses. 2020;12:1420.
14. Albert E, Torres I, Bueno F, Huntley D, Molla E, Fernandez-Fuentes MA, Martinez M, Poujois S, Forque L, Valdivia A, Solano de la Asuncion C, Ferrer J, Colomina J, Navarro D. Field evaluation of a rapid antigen test (Panbio COVID-19 Ag rapid test device) for COVID-19 diagnosis in primary healthcare centres. Clin Microbiol Infect. 2021;27:e7–10.
15. Candel FJ, Barreiro P, San Roman J, Abanades JC, Barba R, Barberan J, Bibiano C, Canora J, Canton R, Calvo C, Carretero M, Cava F, Delgado R, Garcia-Rodriguez J, Gonzalez Del Castillo J, Gonzalez de Villaumbrosia C, Hernandez M, Losa JE, Martinez-Peromingo FJ, Molero JM, Munoz P, Onecha E, Onoda M, Rodriguez J, Sanchez-Celaya M, Serra JA, Zapatero A. Recommendations for use of antigenic tests in the diagnosis of acute SARS-CoV-2 infection in the second pandemic wave: attitude in different clinical settings. Rev Esp Quimioter. 2020;33:466–84.
16. European comission. Commission recommendation of 18.11.2020 on the use of rapid antigen tests for the diagnosis of SARS-CoV-2 infection. https://ec.europa.eu/health/sites/health/files/preparedness_response/docs/sarscov2_rapidantigentests_recommendation_en.pdf. Accessed 8 Nov 2020.
17. European Centre for Disease Prevention and Control. Options for the use of rapid antigen tests for COVID-19 in the EU/EEA and the UK. TECHNICAL REPORT. https://www.ecdc.europa.eu/en/publications-data/options-use-rapid-antigentests-covid-19-eueea-and-uk. Accessed 28 Oct 2020.
18. Marks M, Millat-Martinez P, Ouchi D, Roberts CH, Alemany A, Corbacho-Monne M, Ubals M, Tobias A, Tebe C, Ballana E, Bassat Q, Baro B, VallMayans M, G Beiras C, Prat N, Ara J, Clotet B, Mitja O. Transmission of COVID-19 in 282 clusters in Catalonia, Spain: a cohort study. Lancet Infect Dis. 2021;21:629–36.
19. Weiss A, Jellingso M, Sommer MOA. Spatial and temporal dynamics of SARS-CoV-2 in COVID-19 patients: a systematic review and meta-analysis. EBioMedicine. 2020;58: 102916.
20. Arons MM, Hatfield KM, Reddy SC, Kimball A, James A, Jacobs JR, Taylor J, Spicer K, Bardossy AC, Oakley LP, Tanwar S, Dyal JW, Harney J, Chisty Z, Bell JM, Methner M, Paul P, Carlson CM, McLaughlin HP, Thornburg N, Tong S, Tamin A, Tao Y, Uehara A, Harcourt J, Clark S, Brostrom-Smith C, Page LC, Kay M, Lewis J, Montgomery P, Stone ND, Clark TA, Honein MA, Duchin JS, Jernigan JA, Public H-S, King C, Team CC-I. Presymptomatic SARS-CoV-2 Infections and Transmission in a Skilled Nursing Facility. N Engl J Med. 2020;382:2081–90.
21. Dinnes J, Deeks JJ, Adriano A, Berhane S, Davenport C, Dittrich S, Emperador D, Takwoingi Y, Cunningham J, Beese S, Dretzke J, Ferrante di Ruffano L, Harris IM, Price MJ, Taylor-Phillips S, Hooft L, Leeflang MM, Spijker R, Van den Bruel A, Cochrane C-DTAG. Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection. Cochrane Database Syst Rev. 2020;8:013705.
22. La Scola B, Le Bideau M, Andreani J, 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. 2020;39:1059–61. https://doi.org/10.1007/s10096-020-03913-9.

23. Anika S, Monika P, Andre C, Jamie LB, Vanessa S, Joanna E, Shamez L, Maria Z, Robin G. Duration of infectiousness and correlation with RT-PCR cycle threshold values in cases of COVID-19. Euro Surveill. 2020. https://doi.org/10.2807/1560-7917.ES.2020.25.32.2001483.
24. Kretschmer A, Kossow A, Grüne B, Schildgen O, Mathes T, Schildgen V. False positive rapid antigen tests for SARS-CoV-2 in the real-world and their economic burden. J Infect. 2022;84:248–88. https://doi.org/10.1016/j.jinf.2021.08.020 (**Epub 2021 Aug 17**).
25. World Health Organization. Antigen-detection in the diagnosis of SARS- CoV-2 infection using rapid immunoassays. https://www.who.int/publications/i/item/antigen-detection-in-the-diagnosis-of-sars-cov2infection-using-rapid-immunoassays. Accessed 11 Sept 2020.

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