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Comparative Evaluation of Different SARS-CoV-2 Rapid Point-of-Care Antigen Tests with SARS-CoV-2 PCR for Diagnosis of COVID-19

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Abstract

BACKGROUND: Detection of positive 2019-nCoV nucleic acids by real-time reverse transcriptase-polymerase chain reaction (rRT-PCR)-based assays performed on the upper and lower respiratory samples remains the gold standard for the diagnosis of COVID-19. However, antigen-detecting rapid diagnostic tests can offer a faster (15–30 min) and less expensive way to diagnose active severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection than nucleic acid amplification tests.

AIM: Hence, the present study aimed to compare and evaluate the results of different SARS-CoV-2 rapid point-of-care antigen tests with SARS-CoV-2 PCR as a reference method.

METHODS: Sixty-five nasopharyngeal swab specimens were collected from attendees of the Reference Laboratory of Egyptian university hospitals. The samples were placed in viral transport medium for RNA extraction. The remaining part of the suspension was stored at −70°C until use for COVID-19 antigen testing. All samples were processed for the COVID-19 Ag rapid test and RT-PCR simultaneously.

RESULTS: RT-PCR assay revealed 46 (70.8%) positive samples and 19 (29.2%) negative samples for COVID-19. All eight rapid antigen assays indicated specificity and positive predictive value of 100% each. As for the other parameters, the sensitivity, negative predictive value (NPV), and accuracy ranged from 43.8 to 93.8, 33.3 to 90, and 60 to 96, respectively. Biozak exhibited the best performance with the highest sensitivities 91.3, 81.8, and 93.75, respectively, while Viro and Standard Q were the worst among the tested kits with sensitivity, NPV, and accuracy of 50, 33.3, and 60 each. Regarding the relationship between the viral load of COVID-19 detected by RT-PCR and the results of the eight rapid antigen tests (RAT), we deduced that the higher the viral load, the better the sensitivity observed.

CONCLUSION: The RATs used, in our study, exhibited heterogeneous diagnostic performance, where some of them showed very promising results in comparison to the reference RT-PCR assay.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) belongs to the Coronaviridae family [1]. To this day, three coronaviruses were responsible for outbreaks of severe acute respiratory syndrome with significant morbidities and mortality, those are; SARS-CoV which first appeared in 2002, Guangdong, China, MERS-CoV in Saudi Arabia in 2012 and finally SARS-CoV-2, which emerged in Wuhan, China, at the end of 2019 and has caused the global pandemic [2]. The first discovered cases belonged to patients suffering from contagious viral pneumonia [3]. Only a few weeks later, on 30 January 2020, the WHO declared a global health emergency caused by SARS-CoV-2 [4].

On February 14, 2020, Egypt's health ministry reported the first case in the country that was discovered at the Cairo International Airport involving a Chinese national, and the COVID-19 pandemic was confirmed to have reached Egypt, on March 8, 2020, the first confirmed death was reported [5].

Coronavirus disease 2019 (COVID-19) has a very wide spectrum of clinical manifestations ranging from being an asymptomatic infection or a mild upper respiratory tract disease to severe fatal viral pneumonia with acute respiratory syndrome. Subclinical infections are one of the main concerns of COVID-19 as carriers might spread the infection and remain undiagnosed [6]. Hence, reliable and rapid diagnostic technologies remain a high priority to contain emerging pandemics [7].

Various diagnostic tests are available for the detection of SARS-CoV-2, including nucleic acid amplification testing (NAAT), serological tests,

point-of-care tests, and next-generation sequencing (NGS) [8]. The main testing approaches involve the detection of the virus itself (viral RNA or antigen) or detecting the host immune response to infection (antibodies or other biomarkers). Whole blood, serum, or plasma are used as a specimen for antibody-based immunoassays, and upper or lower respiratory samples are used for antigen-based immunoassays and NAAT [9].

The primary NAAT method is real-time reverse transcriptase-polymerase chain reaction (RT-PCR), is considered the gold standard for SARS-CoV-2 detection, and uses several targeted genomic regions in the molecular diagnosis of virus RNA including the ORF1b or ORF8 regions, the spike protein (S), the nucleocapsid protein (N), the envelope (E), and the RNA-dependent RNA polymerase (RdRP) genes. The serological tests measuring binding antibodies (total immunoglobulins (Ig), IgG, IgM, or IgA) make use of the enzyme-linked immunosorbent assay, chemiluminescent immune-assays for quantitative detection, and lateral flow immunoassays (LFIA) for the rapid qualitative detection of SARS-CoV-2 [10].

Although RT-PCR is considered to be the gold standard for the detection of SARS-CoV-2, this assay has some limitations [11]. They generally take an average of 2–3 h to generate results and PCR tests require certified laboratories, expensive equipment, and trained technicians to operate [12]. On the other hand, antigen testing depends on the direct detection of SARS-CoV-2 proteins (spike or nucleocapsid) using LFIA [13].

Antigen detection rapid diagnostic tests (Ag-RDTs) can offer a faster (15–30 min) and less expensive way to diagnose active SARS-CoV-2 infection than nucleic acid amplification tests. Ag-RDTs perform best in people with a high viral load, early in the course of infection; Ag-RDTs should be prioritized for use in symptomatic people and to test asymptomatic people at high risk of infection, including contacts and health workers, particularly in settings where the capacity to test NAAT is limited [14].

In this study, we will compare the results of different SARS-CoV-2 rapid antigen tests (RATs) and RT-PCR assays.

Objectives

This study aimed to compare and evaluate the results of different SARS-CoV-2 rapid point-of-care antigen tests with SARS-CoV-2 PCR as a reference method and to determine the relationship between the viral load detected by COVID-19 PCR and the results of the eight RATs.

Study design

This study was cross-sectional study.

Materials and Methods

A total of 65 nasopharyngeal swab specimens were collected from attendees of the outpatient clinic at the Reference Laboratory of Egyptian university hospitals (RLEUH). The samples were placed in a viral transport medium for RNA extraction. The remaining part of the suspension was stored at −70°C until use for the COVID-19 antigen test. In this study, samples were divided into two groups: positive RT-PCR (n = 46) for SARS-CoV-2 and negative RT-PCR (n = 19) for SARS-CoV-2. The study was conducted during the period from November 2021 to February 2022. Informed consent was obtained from each participant and the study was approved by the Ethics Committee of the Supreme Council of University Hospitals 2020. The results of the lateral flow immunochromatographic assays were compared with real-time PCR as a reference method.

Lateral flow immunochromatographic assays (LFA)

In this study, eight rapid lateral flow immunochromatographic antigen assays were used for qualitative rapid detection of the SARS-CoV-2 antigen; Abbot Panbio COVID-19 Ag Rapid (Abbott Rapid Diagnostics Jena GmbH, Germany), Roche SARS-CoV-2 Antigen Test (Roche Diagnostics USA), Biozek COVID-19 Antigen Rapid Test (Inzek International Trading, the Netherlands), PCL COVID19 AG GOLD Rapid Test (Pcl Inc., South Korea), the STANDARD TM Q COVID-19 Ag Test (SD Biosensor, Inc., Republic of Korea), DIXION COVID-19 RAPID TEST (Bi medis, Germany), Healgen Coronavirus Antigen Rapid Test Cassette (Swab) – SARS-Cov-2 (Healgen Scientific LLC, USA), and COVID-VIRO®(AAZ-LMB, France).

Lateral flow immunochromatographic antigen assays detect the CoV-2 nucleocapsid (N) antigen in respiratory specimens. All tests were performed according to the manufacturer's instructions and read after 15–30 min. The interpretation of the results was as follows; a colored line should always appear in the control (C) region for the test to be valid. Positive Result: Two colored lines appear, one in the control region and one in the test region. A positive result indicates the detection of SARS-CoV-2 antigens in the sample. Negative Result: A colored line appears in the Control (C) region and no line appears in the Test (T) region. A negative result indicates that the detection threshold of SARS-CoV-2 antigens in the sample has not been reached. Invalid Result: The control line does not appear.

RT-PCR assay

RT-PCR was carried out using the Allplex™ 2019-nCoV Assay kit (Seegene, Seoul, Republic

of Korea). The assay was performed according to the manufacturer's protocol. The test is designed to detect RdRP, nucleocapsid (N) genes specific for SARS-CoV-2, and the envelope gene (E). Nucleic acid extraction was performed on Microlab NIMBUS IVD. Amplification of the target viral genes was performed on CFX96™ Real-Time PCR Detection System (Bio-Rad, Hercules, CA, USA) [15]. According to the manufacturer's recommendations, results were interpreted as follows; positive if the cycle threshold (CT) values of all three target genes were within the cutoff (<40) and negative if all were outside the cut-off or if there was no amplification; otherwise, the result was interpreted as inconclusive [16], [17].

Statistical analysis

Data will be analyzed using the Statistical Package for the Social Sciences software version 25. Frequency (count) and relative frequency (percentage) are used for the categorical data. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) will be calculated, along with the 95% confidence interval. The measurement agreements between tests are to be evaluated with Cohen's kappa (κ) statistics. The comparison between the categorical data will be done using the Chi-square (χ^2) test. Fisher's exact test will instead be used when the expected frequency is <5. $p \leq 0.05$ is considered statistically significant.

Results

A total of 65 nasopharyngeal samples for COVID-19 were tested by RT-PCR taken as our reference method and eight different rapid COVID-19 antigen tests. The 65 samples were not analyzed by all RATs due to inaccessibility and unavailability.

Performance of results of detection of COVID-19 antigen by the eight rapid COVID-19 antigen tests versus RT-PCR

Our reference RT-PCR assay revealed 46 (70.8%) positive samples and 19 (29.2%) negative samples for COVID-19. It was noted that all eight rapid antigen assays showed specificity and PPV of 100% each. As for the other parameters, the sensitivity, NPV, and accuracy ranged from 43.8 to 93.8, 33.3 to 90, and 60 to 96, respectively. Biozak exhibited the best performance with the highest sensitivities, NPV, and accuracy of 91.3, 81.8, and 93.75, respectively. This assay had the highest significant association with our PCR with phi = 0.864, while Viro and Standard Q were the worst among the tested kits with sensitivity, NPV,

and accuracy of 50, 33.3, and 60 each. Thus, they had a non-significant association with PCR with Phi = 0.408 each. None of the specimens results in an invalid test, which would be indicated by a lack of the control line.

The association between COVID-19 RT-PCR and the eight rapid COVID-19 antigen tests and their diagnostic performance is summarized in (Tables 1 and 2).

Table 1: Association between COVID-19 reverse transcriptase-polymerase chain reaction and the eight COVID-19 rapid antigen tests studied

Name of kit used	RT-PCR (%)		Total	Phi	p	Significant
	Negative	Positive				
Abbott						
Negative	19 (29.2)	15 (23.1)	34 (52.3)	0.614	0.001	S
Positive	0	31 (47.7)	31 (47.7)			
Total	19 (29.2)	46 (70.8)	65 (100)			
Biozak						
Negative	9 (28.1)	2 (6.3)	11 (34.4)	0.864	0.0001	S
Positive	0	21 (65.6)	21 (65.6)			
Total	9 (28.1)	23 (71.9)	32 (100)			
PCL						
Negative	4 (20)	4 (20)	8 (40)	0.612	0.006	S
Positive	0	12 (60)	12 (60)			
Total	4 (20)	16 (80)	20 (100)			
Healgen						
Negative	4 (20)	4 (20)	8 (40)	0.612	0.006	S
Positive	0	12 (60)	12 (60)			
Total	4 (20)	16 (80)	20 (100)			
Dixion						
Negative	9 (36)	9 (36)	18 (72)	0.468	0.019	S
Positive	0	7 (28)	7 (28)			
Total	9 (36)	16 (64)	25 (100)			
Roche						
Negative	10 (28.6)	8 (22.8)	18 (51.4)	0.615	0.0001	S
Positive	0	17 (48.6)	17 (48.6)			
Total	10 (28.6)	25 (71.4)	35 (100)			
Standard Q						
Negative	4 (20)	8 (40)	12 (60)	0.408	0.068	NS
Positive	0	8 (40)	8 (40)			
Total	4 (20)	16 (80)	20 (100)			
Viro						
Negative	4 (20)	8 (40)	12 (60)	0.408	0.068	NS
Positive	0	8 (40)	8 (40)			
Total	4 (20)	16 (80)	20 (100)			

*S, NS. Phi: < 0.1: Weak relationship, 0.1–0.3: Moderate relationship, > 0.3: Strong relationship. RT-PCR: Reverse transcriptase-polymerase chain reaction, S: Significant, NS: Non-significant.

Relation between the viral load of COVID-19 detected by RT-PCR and the results of the eight RATs

We divided our samples into two groups according to the viral load obtained by RT- PCR. Group 1 represented samples with a high viral load of CT <25 and Group 2 those with a low viral load of CT >25.

We calculate the sensitivities of the eight RATs among each group. Based on our results, we deduced that the higher the viral load, the better the sensitivity

Table 2: Diagnostic performance of the COVID-19 rapid antigen tests studied compared to the reverse transcriptase-polymerase chain reaction assay as a reference method

COVID-19 antigen detection kits	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Abbott	67.4	100	100	55.9	76.9
Biozak	91.3	100	100	81.8	93.75
PCL	75	100	100	50	80
Healgen	75	100	100	50	80
Dixion	43.8	100	100	50	64
Roche	68	100	100	55.6	77
Standard Q	50	100	100	33.3	60
Viro	50	100	100	33.3	60

PPV: Positive predictive value, NPV: Negative predictive value.

noted. We observed that four kits (Abbott, Roche, Standard Q, and Viro) showed a significant difference in their sensitivities between the two groups with much better performance in Group 1. Table 3 summarizes the rest of the results.

Table 3: Relation between the viral load of COVID-19 detected by reverse transcriptase-polymerase chain reaction and the results of the eight rapid antigen tests

Name of kit used	PCR viral load groups (%)			p
	Group 1 High viral load (CT <25)	Group 2 Intermediate to low viral load (CT >25)	Total	
Abbott				
Negative	1 (4.2)	14 (63.6)	15 (32.6)	0.000
Positive	23 (95.8)	8 (36.4)	31 (67.4)	
Total	24 (100.0)	22 (100)	46 (100)	
Sensitivity (%)	95.8	36.4	67.4	
Biozak				
Negative (%)	0	2 (22.2)	2 (8.7)	0.65
Positive (%)	14 (100)	7 (77.8)	21 (91.3)	
Total (%)	14 (100)	9 (100)	23 (100)	
Sensitivity (%)	100	77.8	91.3	
PCL				
Negative (%)	1 (11.1)	3 (42.9)	4 (25)	0.146
Positive (%)	8 (88.9)	4 (54.1)	12 (75)	
Total (%)	9 (100)	7 (100)	16 (100)	
Sensitivity (%)	88.9	57.1	75	
Healgen				
Negative (%)	1 (11.1)	3 (42.9)	4 (25)	0.146
Positive (%)	8 (88.9)	4 (54.1)	12 (75)	
Total (%)	9 (100)	7 (100)	16 (100)	
Sensitivity (%)	88.9	57.1	75	
Dixion				
Negative (%)	4 (40)	5 (83.3)	9 (56.3)	0.091
Positive (%)	6 (60)	1 (16.7)	7 (43.8)	
Total (%)	10 (100)	6 (100)	16 (100)	
Sensitivity (%)	60	16.7	43.8	
Roche				
Negative (%)	0	8 (53.3)	8 (32)	0.005
Positive (%)	10 (100)	7 (46.7)	17 (68)	
Total (%)	10 (100)	15 (100)	25 (100)	
Sensitivity (%)	100	46.7	68	
Standard Q				
Negative (%)	1 (14.3)	7 (77.8)	8 (50)	0.012
Positive (%)	6 (85.7)	2 (22.2)	8 (50)	
Total (%)	7 (100)	9 (100)	16 (100)	
Sensitivity (%)	85.7	22.2	50	
Viro				
Negative (%)	1 (14.3)	7 (77.8)	8 (50)	0.012
Positive (%)	6 (85.7)	2 (22.2)	8 (50)	
Total (%)	7 (100)	9 (100)	16 (100)	
Sensitivity (%)	85.7	22.2	50	

CT: Cycle threshold, PCR: Polymerase chain reaction.

Discussion

There is an urgent need for point-of-care tests that can be easily and readily available to be used in a health-care setting to generate accurate results within a few hours. These tests should also provide reliable results in the context to facilitate diagnosis and rapid decision-making regarding patient treatment and isolation [18].

Several diagnostic tests are available to identify SARS-CoV-2, including nucleic acid amplification NAAT, serological tests, point-of-care tests, and NGS. The main testing approaches involve the detection of the virus itself (viral RNA or antigen) or detecting the host immune response to infection (antibodies or other biomarkers) [8].

Detection of positive 2019-nCoV nucleic acids by (rRT-PCR)-based assays performed on the upper and lower respiratory samples remains the gold standard for the diagnosis of COVID-19 [19].

Even though RT-PCR is considered the gold standard for SARS-CoV-2 detection, however, real-time PCR test assays have some limitations [11]. On average, they take 2 h to generate results and PCR tests require certified laboratories, expensive equipment, and trained technicians to operate [12]. Antigen testing relies on direct detection of SARS-CoV-2 proteins (spike or nucleocapsid) using LFIA [13].

RATs can offer a faster (15–30 min) and less expensive way of diagnosing active SARS-CoV-2 infection than nucleic acid amplification tests [14].

Therefore, in the present study, we aimed the comparison and evaluation the results of SARS-CoV-2 RT-PCR as a reference method and eight rapid lateral flow immunochromatographic antigen assays; Abbot Panbio COVID-19 Ag Rapid (Abbott Rapid Diagnostics Jena GmbH, Germany), Roche SARS-CoV-2 Antigen Test (Roche Diagnostics, USA), Biozek COVID-19 Antigen Rapid test (Inzek International trading, Netherlands), PCL COVID-19 AG GOLD Rapid Test (Pcl Inc., South Korea), the STANDARDTM Q COVID-19 Ag Test (SD Biosensor, Inc., Republic of Korea), DIXION COVID-19 RAPID TEST, (Bi medis, Germany), Healgen Coronavirus Antigen Rapid Test Cassette (Swab) – SARS-CoV-2 (Healgen Scientific LLC, USA), and COVID-VIRO®(AAZ-LMB, France).

A total of 65 nasopharyngeal swab specimens were collected from attendees of the outpatient clinic at the RLEUH during the period from November 2021 to February 2022.

Regarding the results of our study, the RT-PCR assay revealed 46 (70.8%) positive samples and 19 (29.2%) negative samples for COVID-19. It was noted that all eight rapid antigen assays showed specificity and PPV of 100% each.

Similar to our results, a prospective cohort study by Chu V *et al.* (2022) [20] of 225 adults and children with RT-PCR confirmed SARS-CoV-2 infection, antigen test assays resulted in high specificity of 97%. Another study by Peña *et al.* [21] evaluated the performance of the SARS-CoV-2 rapid antigen test (SD Biosensor, Inc. Republic of Korea) compared with the real-time RT-PCR for SARS-CoV-2 detection among individuals at Iquique city, Tarapacá Region, Chile, revealed also a high specificity of the antigen test reaching 99.6%.

As for the other parameters in the present study, the sensitivity, NPV, and accuracy ranged from 43.8 to 93.8, 33.3 to 90, and 60 to 96, respectively. Biozak exhibited the best performance with the highest sensitivities, NPV, and accuracy of 91.3, 81.8, and 93.75, respectively. This assay had the highest significant association with our PCR with a phi = 0.864.

In line with our study, a study done at the School of Medicine of the National and Kapodistrian University

of Athens compared the diagnostic performance of 14 RATs with RT-PCR, the average sensitivity of all RATs was 88.2% and 80.0%, respectively. However, when only the five best RATS were considered that the sensitivity was found to be as high as 99.1% (for CT ≤30) and 90.9% (for cT ≤33) [22].

In contrast to a study by Landaas *et al.* [23], when comparing RATs with PT-PCR, the overall sensitivity of the RATs was low at 74%. However, they attributed this low sensitivity to an increase in the number of asymptomatic patients in their collected samples and a decrease in viral load in the sample. Similar to this study, our study showed that Varo and standard Q were the worst among the kits with sensitivity, NPV, and accuracy of 50, 33.3, and 60 each. Thus, they had a non-significant association with PCR with Phi = 0.408 each.

Our study was carried out on a small number of samples; therefore, the low sensitivity of some RATs could be attributed to the decreased number of samples taken from symptomatic patients or due to the low viral loads in some samples. Furthermore, low diagnostic sensitivity may be attributed to impaired timing of the sampling relative to the course of the disease, inappropriate sampling technique, type of used swabs, and transportation media [24].

However, in another study by Chimayo *et al.* (2022) [25] the rapid detection test of SARS-CoV-2 antigen by standard Q COVID-19 antigen detection kit, was compared with the real-time RT-PCR test, for the detection of SARS-CoV-2 in respiratory samples, showed a high sensitivity of 98.33% (95% CI, 91.06-99.96%). This high sensitivity may be attributed to the fact that samples were collected from patients highly suspected of having COVID 19 with high viral loads in the samples used. This high sensitivity may be attributed to the fact that samples were collected from patients highly suspected of having COVID-19 with high viral loads in the samples used.

RATs provide fast results but have been criticized, as shown in some studies, for their low sensitivity in samples with low viral loads. Many studies have suggested that the SARS-CoV-2 viral load might predict the severity of the disease and its transmission. Moreover, a higher viral load was related to increasing emergency care needs, and an overall poor prognosis [26].

Therefore, in the present study, we studied the relationship between the viral load of COVID-19 detected by RT-PCR and the results of the eight RATs. We divided our samples into two groups according to the viral load obtained by RT-PCR. Group 1 represented samples with a high viral load of CT <25 and Group 2 those with a low viral load of CT >25.

The sensitivities of the eight RATs among each group were calculated. We observed that four kits (Abbott, Roche, Standard Q, and Varo) showed a significant difference in their sensitivities among the

two groups with much better performance in Group 1. Based on our results, we deduced that the higher the viral load, the better the sensitivity of the rapid antigen test used. Although some tests exhibited significantly low sensitivities in low viral load samples, the number of samples is too small to judge that these tests are not suitable for the diagnosis of SARS-Cov-2. Therefore, before issuing our judgment, more studies must be done on a larger scale. The fact that sensitivity of RAT increases with increased viral loads and in symptomatic patients and *vice versa* is also confirmed by many studies such as that by Chu V *et al.*, Peña *et al.*, Landaas *et al.*, and Jegerlehner *et al.* [20], [21], [23], [27].

As the sensitivity of RATs decreases with low viral loads, false-negative results also increase in these cases, as evident in our study, Abbott, Roche, Standard Q, and Varo RATs showed that the number of false negative results is high in low/intermediate viral load samples and is lowest in high viral load samples. These results support the fact that RATs might have a significant impact on the correct identification of asymptomatic carriers and patients with low viral loads in areas that lack suitable laboratories to perform SARS-CoV-2 real-time RT-PCR diagnostics.

Our results suggest that the RATs, besides their low cost and ease of use, can identify COVID-19-infected patients. However, their analytic sensitivity varies from one manufacturer to another. Thus, the more sensitive RATs can detect the most infected individuals, and thus, they are of great use in congregate settings, such as long-term care facilities, workplaces, schools, and faculties. However, due to discrepancies in the performance of different tests, a careful selection of RATs that meet the best criteria to confer high sensitivity is required.

Finally, it should be noted that the present study has some limitations; first, the sample size tested was small. Second, there was no clinical data on the patients, whether they were symptomatic or asymptomatic, so we could not verify the clinical performance of the test assays. Third, the fluctuant pandemic situation has led to an interrupted availability of the test assays, so it was not possible to evaluate the same number of samples for all kits.

Conclusion

The RATs used in our study exhibited a heterogeneous diagnostic performance, where some of them showed very promising results compared to the reference RT-PCR assay, Biota exhibited the best performance with the highest sensitivities, NPV, and accuracy of 91.3, 81.8, and 93.75, respectively. This assay had the highest significant association with our PCR with phi = 0.864. This could justify its use in some settings, where molecular assays (RT-PCR) are not

available, considering limitations about false-negative results. However, other tests were inferior and failed to provide valid and reliable results, indicating that they are not good alternatives for automated methods.

Considering the current results, we must be cautious about the routine use of these low-sensitivity tests for critical decision-making for clinicians. Thus, we recommend more larger-scale studies involving patients with known status and symptoms of the disease.

Finally, it is important to be aware of the limitations of different RATs and to bear in mind that their sensitivity is lower than that of the well-established and gold standard RT-PCR molecular assay. Nevertheless, in some situations, this might be outweighed by the advantages of the faster identification of infected individuals and thus allowing for rapid isolation to prevent further transmission and spread of the disease.

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