RESEARCH ARTICLE / ARAŞTIRMA

DOI: 10.4274/mjima.galenos.2021.2021.2
Mediterr J Infect Microb Antimicrob 2022;11:2
Erişim: http://dx.doi.org/10.4274/mjima.galenos.2021.2021.2

Value of Rapid Antigen Test in Comparison with Reverse Transcriptase-Polymerase Chain Reaction Method in the Diagnosis of COVID-19

COVID-19 Teşhisinde Ters Transkriptaz-Polimeraz Zincir Reaksiyonu Yöntemine Kıyasla Hızlı Antijen Testinin Değeri

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Abstract

Introduction: Using the rapid antigen test (RAT) before exhausting the reverse transcriptase-polymerase chain reaction (RT-PCR) test's capacity is crucial to enhance suitable detection of patients and timely reception of results. Therefore, this study was done to evaluate the sensitivity and specificity of RAT and compare it with the RT-PCR method in the diagnosis of Coronavirus disease-2019 (COVID-19).

Materials and Methods: This study was performed on 634 individuals referred to public sampling centers performing the COVID-19 test in Shiraz City, Fars Province, Southern Iran. The sampling process was done following a multi-stage stratified protocol. The COVITECH® one-step real-time RT-PCR kit method as the reference standard test was compared with the RAT using E-Health Barakat Company® rapid antigen kit in the pharyngeal specimens. The trained personnel collected the data. Sensitivity, specificity, positive predictive value (PPV), negative predictive value, and the accuracy of the RAT were calculated using the MedCalc software. Moreover, the Kappa value was used to assess the level of agreement between RT-PCR and RAT.

Results: According to the results of the RT-PCR method as a reference test; sensitivity, specificity, Kappa value, and accuracy of the RAT were 81.82%, 92.28%, 63.8%, and 91.01%, respectively in the diagnosis of COVID-19. In asymptomatic individuals, the specificity and the PPV of the RAT were 100%.

Conclusion: In conclusion, our results suggested that a positive RAT provides considerable information for diagnosing COVID-19 in adults. As a result, in general, due to the high sensitivity, specificity, and accuracy of the RAT, it can be replaced with the RT-PCR test considering factors such as time, cost, and speed.

Keywords: COVID-19, reverse transcriptase polymerase chain reaction, sensitivity, specificity, rapid

Cite this article as: Mirahmadizadeh A, Yeganeh BS, Hassanzadeh J, Badiee L, Vali M, Maleki Z, Akbari A, Pakdel T, Ghaem H. Value of Rapid Antigen Test in Comparison with Reverse Transcriptase-Polymerase Chain Reaction Method in the Diagnosis of COVID-19. Mediterr J Infect Microb Antimicrob. 2022;11:2.

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Received/Geliş Tarihi: 28.05.2021 **Accepted/Kabul Tarihi:** 01.11.2021

Published: 6 January 2022

Öz

Giriş: Ters transkriptaz-polimeraz zincir reaksiyonu (RT-PCR) testinin kapasitesi tükenmeden hızlı antijen testinin (RAT) kullanılması, olguların uygun şekilde saptanması ve sonuçların zamanında alınması için çok önemlidir. Bu nedenle, bu çalışma, Koronavirüs hastalığı-2019 (COVID-19) tanısında RAT'nin duyarlılığını ve özgüllüğünü değerlendirmek ve RAT'ı RT-PCR yöntemiyle karşılaştırmak için yapılmıştır.
Gereç ve Yöntem: Bu uyum çalışması, İran'ın güneyindeki Fars eyaleti, Şiraz şehrinde COVID-19 testi yapan halk örnekleme merkezlerine sevk edilen 634 kişi üzerinde gerçekleştirildi. Örnekleme işlemi, çok aşamalı ve tabakalı bir protokol izlenerek yapıldı. Faringeal numunelerde referans standart test olarak COVITECH® tek adımlı gerçek zamanlı RT-PCR kiti yöntemi kullanıldı ve E-Health Barakat Company® hızlı antijen kitini kullanan RAT ile karşılaştırma yapıldı. Eğitimli personel verileri topladı. Duyarlılık, özgüllük, pozitif prediktif değer, negatif prediktif değer ve RAT'ın doğruluğu MedCalc yazılımı kullanılarak hesaplandı. Ayrıca, RT-PCR ve RAT arasındaki uyum düzeyini değerlendirmek için Kappa değeri kullanıldı.
Bulgular: Referans test olarak RT-PCR yönteminin sonuçlarına göre, COVID-19 tanısında duyarlılık, özgüllük, Kappa değeri ve RAT'nin doğruluğu sırasıyla %81,82, %92,28, %63,8 ve %91,01 olarak bulundu. Asemptomatik bireylerde, RAT'ın özgüllüğü ve pozitif prediktif değeri %100 olarak gösterildi.
Sonuç: Sonuç olarak, bulgularımız pozitif bir RAT'ın yetişkinlerde COVID-19 teşhisi için önemli bilgiler sağladığını gösterdi. Genel olarak RAT, yüksek duyarlılığı, özgüllüğü ve doğruluğu nedeniyle zaman, maliyet, hız gibi faktörler göz önünde bulundurulduğunda RT-PCR testinin yerini alabilir.
Anahtar Kelimeler: COVID-19, ters transkriptaz polimeraz zincir reaksiyonu, duyarlılık, özgüllük, hızlı

Introduction

Severe acute respiratory syndrome-Coronavirus-2 (SARS-CoV-2) has recently caused a widespread pandemic with severe consequences for healthcare systems worldwide. In many countries, access to diagnostic tests has faced challenges. Many studies are being conducted to make reliable, inexpensive, and rapid diagnostic tests (RDTs) to detect specific antigens for Coronavirus disease-2019 (COVID-19). Many areas in the United States seek to rapidly expand their testing capabilities for the virus because they believe that diagnostic tests could be a crucial tool in fighting against COVID-19[1,2]. The reverse transcription-polymerase chain reaction (RT-PCR) test used a RT-PCR to detect viral ribonucleic acid[3]. The RT-PCR test has been recently considered as the benchmark for SARS-CoV-2 detection, but no comprehensive evaluation has been done on the potential of using antibody and antigen testing procedures yet[2].

Rapid diagnostic tests are tests that detect direct antigens of SARS-CoV-2 proteins that are found in respiratory secretions. Despite the availability of RDTs, before their application, they need to be thoroughly assessed and compared in terms of their ability to detect SARS CoV-2 antigens[4,5]. Rapid antigen testing (RAT) can enhance the overall functional capacity of the COVID-19 testing centers. It offers several advantages, such as the shorter time needed to obtain results and the reduced costs, especially with a limitation on the capacity of the RT-PCR method. Rapid antigen test reduces disease transmission by more efficiently detecting highly infectious cases and enabling more effective contact tracing[6,7].

So far, COVID-19 has been mostly diagnosed by the RT-PCR method applied on samples from the upper part of the throat[7]. There are various advantages in using RATs compared to RT-PCR for COVID-19 diagnosis. These tests have been designed for both laboratory and clinical use, and their results are usually presented at a low cost within 10-30 min post-analysis. Notably, they have sufficient sensitivity for detecting individuals having high amounts of viral antigens, such as those with symptoms related to the pre-phase of the disease and initial symptoms (until five days after symptom manifestations), and probably greatly contribute to the spread of disease[6,8]. The use of RATs seems essential when the RT-PCR test's capacity is exhausted for early case detection and timely result acquisition. During the COVID-19 pandemic, evaluating the sensitivity and specificity of RAT is essential, given its advantages compared to the RT-PCR test. Therefore, this study was conducted for the first time in Iran to address this research gap and evaluate the sensitivity and specificity of RAT according to its advantages compared to the RT-PCR test for COVID-19 detection.

Materials and Methods

This study was performed on 634 individuals who are referred to the public sampling centers that perform COVID-19 tests in Shiraz city, Fars province, and southern Iran on December 13-18, 2020. The sampling method was done following a multi-stage stratified protocol. First, 10 public sampling centers that perform both RAT and RT-PCR tests were selected. According to the statistics provided by the Deputy of Development, in the next stage, the share proportionate to each of the centers was calculated. Finally, within those centers, patients and their close contacts were randomly selected. The inclusion criterion was the residence of individuals in Shiraz city. The exclusion criteria included incomplete information and conscious disagreement to participate in the study. The required sample size for this study was calculated by the formula used for determining the sample size in agreement studies[2]. A sample size of 300 people

was determined to be appropriate for the study. The sample size was multiplied by 1.5 due to the effect of study design on cluster sampling and stratification; therefore, the final sample size was calculated as 500 people (β=0.20, α=0.01).

This study used a checklist for data collection, which included the following variables: age, sex, contact to any positive cases of COVID-19, pregnancy, travel history in the last two weeks before the positive result, symptoms like fever, sore throat, myalgia, general weakness, diarrhea, nausea, and shortness of breath (dyspnea), and history of underlying diseases including diabetes mellitus, cardiovascular disease, chronic pulmonary disease, hypertension, malignancy, obesity, and smoking status. These variables were assessed using the subgroup analysis. Additionally, the RT-PCR test results were considered as the gold standard and compared with the RAT results. In a center that operates between 8 AM and 10 PM, we conducted PCR and RATs at around 3 PM to 5 PM. The trained personnel collected study data. Quality assurance was performed by the supervision of gathering, extracting, and introducing data into the software and data analysis processes.

Rapid antigen tests were performed on nasopharyngeal specimens by E-Health Barakat Company® rapid antigen kit as a SARS-CoV-2 antigen test, detecting the presence of virus S protein by immunochromatography method[9].

RT-PCR Test

RT-PCR tests were performed on the pharyngeal specimens using COVITECH® one-step real-time RT-PCR kit containing primers and probes of S and E genes for SARS-CoV-2 gene and RNase P detection as the internal control. The resulting cycle threshold values of <35 were considered positive. This test was considered the gold standard for SARS-CoV-2 detection[10].

Statistical Analysis

Descriptive analyses, including frequency and percentage, were used for qualitative variables. According to the RT-PCR outcomes in the role of a standard test, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and precision of fast testing were calculated by the MedCalc software. Moreover, the Kappa value was used to assess the level of agreement between RT-PCR and RAT. A 95% confidence interval (CI) was provided by the Wilson score method. All analyses were performed in the MedCalc software version 11.6.0.0 and Statistical Package for the Social Sciences software version 26.0. P values of <0.05 were considered statistical significance. This study was approved by the Ethics Committee of the Shiraz University of Medical Sciences with the ethics code of IR.SUMS.REC. 1399.1253.

Results

Overall Findings

This study analyzed 634 patients [mean age of 37.98±15.90 years; 61.4% (389/634) were males]. Table 1 shows the demographic information of the participants. Among 634 patients, 77 had positive and 557 had negative RT-PCR results with COVID-19 prevalence of 12.15% (95% CI: 9.70-14.94) (Figure 1). Among 77 patients with positive RT-PCR results, 86.30% (63/77) had positive RAT results. Of 557 individuals with non-positive RT-PCR outcomes, 92.28% (514/557) had negative rapid test results.

Performance of RAT in SARS-CoV-2 Diagnosis

Positive RAT results were determined in 106 patients (<60 years old, n=69; ≥60 years old, n=8; 48 males and 29 females). According to RT-PCR results as the reference test, the sensitivity, specificity, Kappa value, and accuracy of the RAT were equal to 81.82% (95 CI%: 71.38-89.69), 92.28% (95 CI%: 89.74-94.36), 63.8% (95 CI%: 55.2-72.3), and 91.01% (95 CI%: 88.51-93.12) in COVID-19 diagnosis, respectively (Table 2). Patients aged ≥60 years had greater PPV and RAT precision for detecting SARS-CoV-2 compared to individuals aged <60 years. Females showed greater specificity and NPV in the RAT for detecting SARS-CoV-2 than males. For asymptomatic people, the RAT has 100% specificity and 100% PPV, whereas 96.51% specificity and 81.08% PPV in symptomatic individuals. Performance of the RAT in COVID-19 diagnosis in terms of various demographic and clinical characteristics is presented in Table 3. Additionally, Figure 2 shows the receiver operating characteristic curve of the RAT performance in detecting SARS-CoV-2 compared to the RT-PCR as a standard test (area under the curve of 0.87).

Discussion

This study compared the RAT with RT-PCR. First, RAT was found to have a great function for clinic-related purposes, with 81.82% sensitivity and 92.28% specificity. Second, based on our findings, its specificity was very high in asymptomatic individuals (100%).

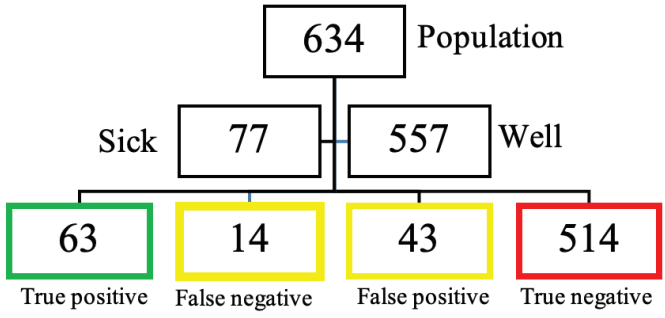

Figure 1. Flowchart of the study

With the spread of SARS-CoV-2, there will be an increasing inconsistency between the count of required testing procedures and the capability of labs or major health care clinics[11]. The RAT is performed on-site and is interpreted by minimally trained health workers and does not require special equipment. It has low cost and fast delivery of outcomes compared to the RT-PCR. The previous reports on RATs for SARS-CoV-2 diagnosis have shown their weak function. Therefore, they are not generally applied[12-15]. Some RATs have been indicated to have remarkably higher reliability[16-19]. Despite the promising use of RAT as a part of a larger strategy to detect and control COVID-19[20], preliminary research is needed to confirm their application in different contexts.

Results of the two recent investigations in Spain that consist of 412 (54 RT-PCR positive cases)[16] and 255 patients (60 RT-PCR positive cases)[17] have reported 79.3% and 76.3% sensitivity, respectively for RAT. However, the second research revealed an 86.5% RAT sensitivity in individuals whose symptoms had been

Table 1. Demographic and clinical information of patients participating in the study (n=634)

Variable			No.	%
Demographic	Sex	Male	389	61.4
		Female	245	38.6
	Age (year)	≤18	45	7.1
		19-35	275	43.4
		36-64	275	43.4
		≥65	39	6.2
	Symptoms of COVID-19	Yes	503	79.3
	Contact to a positive case	Yes	152	24.0
	Travel	Yes	80	12.6
Signs and symptoms	Fever	Yes	129	20.3
	Sore throat	Yes	143	22.6
	Myalgia	Yes	260	41.0
	General weakness	Yes	108	17.0
	Diarrhea	Yes	40	6.3
	Nausea	Yes	43	6.8
	Shortness of breath	Yes	1	0.2
Comorbidities	Pregnancy	Yes	1	0.2
	Diabetes mellitus	Yes	42	6.6
	Cardiovascular disease	Yes	32	5.0
	Chronic pulmonary	Yes	10	1.6
	HTN	Yes	58	9.1
	Malignancy	Yes	4	0.6
	Demographic data	Yes	18	2.8
	Demographic data	<30	626	98.7
		≥30	8	1.3

COVID-19: Coronavirus disease-2019, HTN: Hypertension

Table 2. The performance of the rapid test for Coronavirus disease-2019 infection with reverse transcriptase-polymerase chain reaction result as a reference

Variable	RT-PCR									
Rapid test		Positive	Negative	Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Disease prevalence (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Accuracy (95% CI)
	Positive	63	43	81.82% (71.38-89.69)	92.28% (89.74-94.36)	10.60 (7.81-14.39)	0.20 (0.12-0.32)	12.15% (9.70-14.94)	59.43% (51.90-66.55)	97.35% (95.81-98.33)	91.01% (88.51-93.12)
	Negative	14	514								

RT-PCR: Reverse transcriptase-polymerase chain reaction, CI: Confidence interval

Table 3. The performance of rapid test for Coronavirus disease-2019 infection with reverse transcriptase-polymerase chain reaction result as a reference by demographic and clinical information

Variable		Results (n)				Test performance (%)					
		TP	TN	FP	FN	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Accuracy (95% CI)	Kappa (95% CI)
Age (year)	<60	56	465	13	39	58.95 (48.38-68.94)	97.28 (95.39-98.54)	81.16 (71.07-88.31)	92.26 (90.35-93.82)	90.92 (88.27-93.15)	63.2 (54.0-72.3)
	≥60	7	49	1	4	63.64 (30.79-89.07)	98.00 (89.35-99.95)	87.50 (48.87-98.09)	92.45 (84.85-96.40)	91.80 (81.90-97.28)	69.0 (43.8-94.2)
Sex	Male	37	312	11	29	56.06 (43.30-68.26)	96.59 (93.99-98.29)	77.08 (64.43-86.20)	91.50 (89.11-93.39)	89.72 (86.26-92.55)	59.1 (47.7-70.4)
	Female	26	202	3	14	65.00 (48.32-79.37)	98.54 (95.78-99.70)	89.66 (73.37-96.46)	93.52 (90.44-95.66)	93.06 (89.12-95.91)	71.4 (58.7-84.1)
Fever	No	41	421	9	34	54.67 (42.75-66.21)	97.91 (96.06-99.04)	82.00 (69.80-89.98)	92.53 (90.61-94.08)	91.49 (88.70-93.77)	61.0 (50.5-71.5)
	Yes	22	93	5	9	70.97 (51.96-85.78)	94.90 (88.49-98.32)	81.48 (64.53-91.41)	91.18 (85.61-94.72)	89.15 (82.46-93.94)	68.9 (53.8-84.0)
Sore throat	No	51	399	10	31	62.20 (50.81-72.68)	97.56 (95.55-98.82)	83.61 (72.99-90.59)	92.79 (90.69% to 94.44)	91.65 (88.84-93.94)	66.6 (57.1-76.0)
	Yes	12	115	4	12	50.00 (29.12-70.88)	96.64 (91.62-99.08)	75.00 (51.39-89.49)	90.55 (86.51-93.47)	88.81 (82.47-93.47)	53.8 (34.1-73.5)
Myalgia	No	17	329	3	25	40.48 (25.63-56.72)	99.10 (97.38-99.81)	85.00 (63.41-94.88)	92.94 (91.11-94.41)	92.51 (89.36-94.97)	51.3 (35.9-66.7)
	Yes	46	185	11	18	71.88 (59.24-82.40)	94.39 (90.18-97.17)	80.70 (69.77-88.34)	91.13 (87.40-93.84)	88.85 (84.38-92.40)	68.8 (58.3-79.3)
General weakness	No	45	439	8	34	56.96 (45.33-68.06)	98.21 (96.50-99.22)	84.91 (73.38-91.98)	92.81 (90.92-94.33)	92.02 (89.36-94.18)	63.8 (53.9-73.8)
	Yes	18	75	6	9	66.67 (46.04-83.48)	92.59 (84.57-97.23)	75.00 (57.05-87.14)	89.29 (82.97-93.45)	86.11 (78.13-92.01)	61.5 (43.9-79.1)
Diarrhea	No	61	483	13	37	62.24 (51.88-71.84)	97.38 (95.56-98.60)	82.43 (72.86-89.13)	92.88 (91.01-94.39)	91.58 (89.05-93.69)	66.1 (57.5-74.8)
	Yes	2	31	1	6	25.00 (3.19-65.09)	96.88 (83.78-99.92)	66.67 (17.10-95.10)	83.78 (77.51-88.57)	82.50 (67.22-92.66)	28.6 (8.2-65.3)
Nausea	No	60	481	14	36	62.50 (52.03-72.18)	97.17 (95.30-98.45)	81.08 (71.43-88.02)	93.04 (91.16-94.54)	91.54 (89.00-93.66)	65.7 (57.0-74.5)
	Yes	3	33	0	7	30.00 (6.67-65.25)	100.00 (89.42-100.00)	100.00	82.50 (75.86-87.61)	83.72 (69.30-93.19)	39.7 (7.1-72.3)
Shortness of breath	No	63	514	14	42	60.00 (49.98-69.44)	97.35 (95.59-98.54)	81.82 (72.40-88.53)	92.45 (90.64-93.93)	91.15 (88.67-93.25)	64.2 (55.6-72.8)
	Yes	1	1	1	1	50.00 (1.26-98.74)	50.00 (1.26-98.74)	50.00 (12.35-87.65)	50.00 (12.35-87.65)	50.00 (6.76-93.24)	0.0 (-9.8-9.8)
Pregnancy	No	63	514	14	42	60.00 (49.98-69.44)	97.35 (95.59-98.54)	81.82 (72.40-88.53)	92.45 (90.64-93.93)	91.15 (88.67-93.25)	64.2 (55.6-72.8)
	Yes	0	0	0	1	-	-	-	-	-	-
Diabetes mellitus	No	57	480	13	42	57.58 (47.23-67.45)	97.36 (95.53-98.59)	81.43 (71.42-88.50)	91.95 (90.08-93.50)	90.71 (88.08-92.92)	62.2 (53.2-71.3)
	Yes	6	34	1	1	85.71 (42.13-99.64)	97.14 (85.08-99.93)	85.71 (45.92-97.70)	97.14 (84.69-99.52)	95.24 (83.84-99.42)	82.9 (59.8-100.0)

Table 3 Continued

Cardiovascular disease	No	61	488	13	40	60.40 (50.17-69.99)	97.41 (95.60-98.61)	82.43 (72.84-89.14)	92.42 (90.55-93.95)	91.20 (88.64-93.34)	64.7 (56.0-73.4)
	Yes	2	26	1	3	40.00 (5.27-85.34)	96.30 (81.03-99.91)	66.67 (18.10-94.76)	89.66 (80.85-94.68)	87.50 (71.01-96.49)	43.4 (-2.1-88.8)
Chronic pulmonary disease	No	61	508	14	41	59.80 (49.63-69.39)	97.32 (95.54-98.53)	81.33 (71.73-88.21)	92.53 (90.72-94.01)	91.19 (88.68-93.29)	63.9 (55.2-72.6)
	Yes	2	6	0	2	50.00 (6.76-93.24)	100.00 (54.07-100.00)	100.00	75.00 (52.96-88.88)	80.00 (44.39-97.48)	54.5 (4.4-100.0)
HTN	No	57	466	12	14	80.28 (69.14-88.78)	97.49 (95.66-98.70)	82.61 (72.86-89.36)	97.08 (95.42-98.16)	95.26 (93.14-96.88)	78.7 (70.8-86.6)
	Yes	6	48	2	2	75.00 (34.91-96.81)	96.00 (86.29-99.51)	75.00 (42.14-92.51)	96.00 (87.83-98.76)	93.10 (83.27-98.09)	71.0 (44.2-97.8)
Malignancy	No	63	510	14	43	59.43 (49.46-68.87)	97.33 (95.56-98.53)	81.82 (72.39-88.54)	92.22 (90.40-93.73)	90.95 (88.44-93.08)	63.7 (55.1-72.3)
	Yes	0	4	0	0	-	-	-	-	-	-
Smoking	No	63	497	14	42	60.00 (49.98-69.44)	97.26 (95.45-98.49)	81.82 (72.40-88.53)	92.21 (90.35-93.74)	90.91 (88.36-93.06)	64.0 (55.5-72.6)
	Yes	0	17	0	1	0.00 (0.00-97.50)	100.00 (80.49-100.00)	-	94.44 (94.44-94.44)	94.44 (72.71-99.86)	-
BMI	<30	62	508	14	42	59.62 (49.54-69.13)	97.32 (95.54-98.53)	81.58 (72.06-88.38)	92.36 (90.54-93.86)	91.05 (88.54-93.17)	63.8 (55.2-72.5)
	≥30	1	6	0	1	50.00 (1.26-98.74)	100.00 (54.07-100.00)	100.00	85.71 (60.01-96.00)	87.50 (47.35-99.68)	60.0 (7.2-100.0)
Symptoms of COVID-19	No	3	127	0	1	75.00 (19.41-99.37)	100.00 (97.14-100.00)	100.00 -	99.22 (95.88-99.86)	99.24 (95.82-99.98)	85.3 (57.0-100.0)
	Yes	60	387	14	42	58.82 (48.64-68.48)	96.51 (94.21-98.08)	81.08 (71.42-88.03)	90.21 (87.95-92.08)	88.87 (85.79-91.48)	61.6 (52.6-70.7)
Contact	No	44	400	7	31	58.67 (46.70-69.92)	98.28 (96.49-99.31)	86.27 (74.64-93.07)	92.81 (90.78-94.41)	92.12 (89.34-94.36)	65.5 (55.4-75.5)
	Yes	19	114	7	12	61.29 (42.19-78.15)	94.21 (88.44-97.64)	73.08 (55.65-85.45)	90.48 (85.89-93.68)	87.50 (81.17-92.30)	59.0 (42.5-75.6)

TP: True positive, TN: True negative, FP: False-positive, FN: False negative, PPV: Positive predictive value, NPV: Negative predictive value, RT-PCR: Reverse transcription-polymerase chain reaction, CI: Confidence interval

manifested in <7 days[17]. The World Health Organization (WHO) guidelines require the RATs to show a sensitivity of >80% and a specificity of >97% compared to the RT-PCR as a standard test[20]. A study[21] revealed the sensitivity of RAT as remarkably greater in specimens related to patient detection (92.6%) and followed the people in contact with patients (94.2%) than monitoring asymptomatic cases (79.5%). Recently a study[17] revealed a greater sensitivity in symptomatic individuals (85.3%) compared to those asymptomatic (54.5%), which is in line with the recommendation by the WHO in using RATs to screen asymptomatic individuals in communities with a low COVID-19 prevalence because of higher risk of false-positive results[20]. Our study revealed a high specificity in asymptomatic individuals, indicating that the negative results of the RAT test in asymptomatic individuals can be trusted. This could be due to the differences in the type of PCR and RAT performed, as well as differences in the kits used and the time of the two tests.

The function of RATs may be influenced by the epidemiological characteristics of the participants. Thus, epidemiological characteristics in a specific community would determine the type of test application and the procedure of interpreting the outcomes[20]. In communities that face a great disease incidence and number of symptomatic individuals, a positive RAT is considered to confirm the infection; however, if the symptoms are

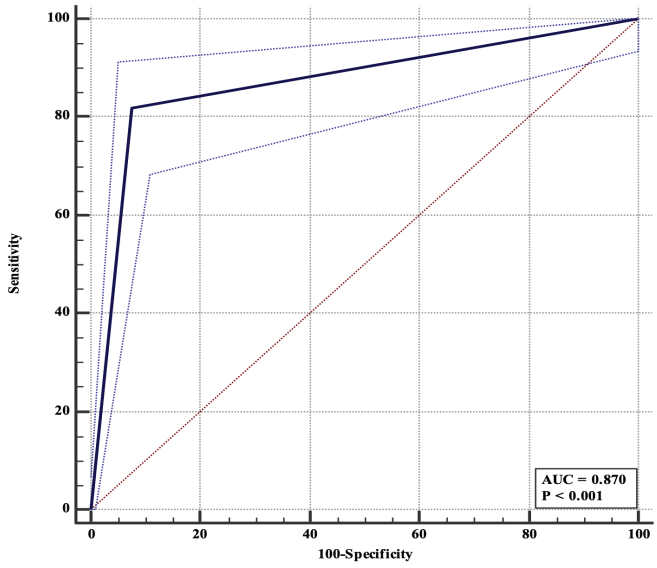

Figure 2. ROC curve regarding RAT for performance for COVID-19 diagnosis compared to the RT-PCR as a reference test

red line: Random classifier, black line: better line of RAT for performance for COVID-19 diagnosis compared to the RT-PCR as a reference test, blue line: CI of better line

consistent with the disease, non-positive outcome results need more evaluation to confirm ventilatory disease-causing agents, such as the RT-PCR for SARS-CoV-2 detection. In communities that face a low disease incidence and asymptomatic individuals, a non-positive result is acceptable. Otherwise, the result may require RT-PCR test confirmation as it may be incorrect.

Using RATs for diagnosis-related purposes highly decreases the load of testing procedures seen in diagnostic labs. Changes within the major health care units are necessary; however, experiencing overloads of patients for COVID-19 testing and diagnosis to equip them with RAT right at the place. This testing process is conducted in health care centers, thus it simplifies the procedure and provides fast results to the physician and patient, thereby improving the decision-making process and reducing the working pressure imposed on healthcare providers. RAT centers are required to completely follow the proper steps needed for biosecurity considerations.

Our findings have instant implications for clinic settings because they revealed that RATs are a valid diagnostic test for timely diagnosis, monitoring, and rein of SARS-CoV-2 transmission.

Therefore, our results revealed that the RAT offers excellent function in clinic settings as a testing procedure for patient care and it yields greater outcomes in asymptomatic individuals. However, the results should be interpreted in the light of the local epidemiological context. The simplicity and speed offered by RAT and its good clinical performance can help prevent higher working loads imposed on the health care system since it is expected to witness the increased number of individuals with ventilatory diseases in labs in winter.

This study was a historical analysis that focused on the probabilistic experience of diagnostic errors, which was the study's primary limitation. Additionally, this research has insufficient data on the severity of infections in the participants and measurements of viral load in the samples, such as a period threshold. Probably, various RT-PCR standards were also a limitation of the study. However, they are all used for routine hospital diagnosis and are all validated and widely used worldwide.

Conclusion

Finally, the current study results revealed that the non-negative outcome of RAT would present remarkable data for detecting COVID-19 in adults. A high total consistency was observed between the RAT and RT-PCR test [Kappa=0.638 (95% CI: 0.552-0.723)]. The RAT can be a confirmation that individuals are healthy and that the false-positive value is 0% due to its high specificity, especially in asymptomatic individuals (whose RAT is negative and are not sick). Therefore, in general, the RAT could be replaced with the RT-PCR test considering factors such as time, cost, and speed, due to its high sensitivity, specificity, and accuracy. Therefore, the RAT test is very reliable if it is negative in asymptomatic individuals.

Acknowledgment

The authors would like to thank the staff of the laboratories in the Shiraz University of Medical Sciences, Shiraz City, Fars Province, Iran.

Ethics

Ethics Committee Approval: The study were approved by the Shiraz University of Medical Sciences of Ethics Committee (protocol number: IR.SUMS.REC.1399.1253, date: 24.02.2021).

Informed Consent: Consent form was filled out by all participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: A.M., H.G., Design: J.H., Data Collection or Processing: B.S.Y., L.B., Analysis or Interpretation: M.V., Z.M., Literature Search: A.A., Writing: M.V., T.P., H.G.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The present study received financial support from the Shiraz University of Medical Sciences (grant number: 22608).

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