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RESEARCH ARTICLE

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The sensitivity and specificity of COVID-19 rapid anti-gene test in comparison to RT-PCR test as a gold standard test

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Abstract

Background: Coronavirus disease 2019 (COVID-19) is a modern infectious disease, first identified in December 2019 in Wuhan, China. The etiology is via severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), in a pandemic manner. The study aimed to compare between RT-PCR and rapid anti-gene tests for COVID-19 with regard to sensitivity and specificity.

Methods: This is a cohort hospital-based study done during the period of July to September 2020. Both rapid anti-gene test kit (SARS-CoV-2) and RT-qPCR were used for the detection of COVID-19 in suspected cases.

Results: A total of 148 cases were tested using both the RT-qPCR and rapid test. Twenty-nine (19.6%) of these cases had positive results for RT-qPCR and 119 (80.4%) were negative, whereas 52 (35.1%) patients were positive to rapid anti-gene test and 96 (64.9%) of them negative. The sensitivity of the rapid test was 37.9%, the specificity was 65.5% and the accuracy was 64.44%. Rapid IgG test was positive in 47 (31.8) of cases. Although, rapid IgM test was positive in 18 (12.2%). The rapid IgG test was more sensitive than rapid IgM (Sensitivity 34.48% vs. 3.45%), but it was less specific than rapid IgM test (Specificity 68.91% vs. 85.71%).

Conclusion: We cannot consider rapid anti-gene test alone as a diagnostic method for COVID-19. We should also conduct RT-PCR test and other investigations like imaging CT scan of chest to confirm the diagnosis. The rapid IgG test is more sensitive than rapid IgM, but it was less specific.

KEYWORDS
COVID-19, rapid anti-gene test, RT-qPCR, SARS-CoV-2

1 | INTRODUCTION

Coronavirus disease (COVID-19) is a very infectious disease due to an old virus. Individuals who fall ill with COVID-19 will be exposed to a wide spectrum of manifestations ranging from mild, moderate, severe or critical, but most of mild symptoms will recover without treatment.[1] The disease spreads very easily especially among those who are physically close via the air, through small droplets, when the infected subjects breathe, talk, sing, cough, and sneeze.[2] Worldwide, there are rapid tests which used to quickly detect IgM-IgG antibodies

against COVID-19[3] and RT-PCR which used to detect SARS-CoV-2, which contains only RNA.[4] Common features of COVID-19 include fever, loss of smell and taste, fatigue, breathing difficulties, and cough. These symptoms might begin 1–14 days after contracting the microbes. Individuals might develop signs of acute respiratory distress syndrome (ARDS). It can be multifactorial and promoted by cytokine storms,[5] septic shock, multiorgan failure, and thromboembolic phenomenon. Longer-term injury to organs (in particular, the lungs and heart) has been reported.[6,7] Coronaviruses are zoonotic, meaning they can be pathogenic to both humans and animals.[8,9]

WHO has acquired different testing protocols for the COVID-19.[10] The standard one is real-time reverse transcription polymerase chain reaction (rRT-PCR).[11] Typically, this test is done by obtaining a sample from a nasopharyngeal swab; however, a sputum sample can also be used.[12,13]

In terms of management, Pakzad and colleagues concluded from large systematic review and meta-analysis that there are higher levels of pathogenic microorganism co-infection among COVID-19 cases, and they support the empirical use of antibacterial, antifungal, and antiviral treatment specifically at the onset of the COVID-19 infection.[14]

Zandi et al., said it is of importance to diagnose the SARS-CoV-2-infected persons early to hinder the virus spreading further, and it could be treated by utilizing the most beneficial detecting method along with the most right sample. In addition, using the most sufficient gene for RT-real-time PCR and considering the onset symptoms is of high importance in the process of diagnosis. They tried to point out the importance of clinical features, diagnosis of SARS-CoV2, and also timing and the samples types in a better distinguishing of infected cases.[15]

In a large meta-analysis, Malekifar et al., systematically searched scientific databases, including Medline, Scopus, WOS, and Embase. They applied the random effects model for pooling all studies. They found 33 studies including 10,484 cases were infected. The viral co-infection estimated prevalence was 12.58%. They concluded the lowest rate of co-infection belonged to respiratory viruses, whereas, blood-borne viruses had the highest rate. Also, they suggested an urgent requirement for further investigation about viral co-infection with SARS-CoV-2, reaching to PCR.[16] Physiologically speaking, SARS-CoV-2, the etiologic agent of COVID-19, has led to a worldwide pandemic with more than 660 million patients with altered in humans' microbiota in COVID-19 patients. This alteration may contribute to the bacterial or viral infections and can mostly affect the immune system.[17]

This study compared between PCR and rapid anti-gene tests used to detection of COVID-19, thus for calculating sensitivity and specificity of these tests.

2 | METHODS

2.1 | Study design and setting

This is a cohort hospital-based study done during the period of July to September 2020. It was performed among COVID-19 patients in Ghazi AL-Hariri Hospital, Baghdad Medical City Complex. About 3440 cases were tested using either RT-PCR or rapid test. A total of 1199 (34.85%) cases were tested using just the rapid test, whereas 2241 (65.15%) cases were tested using the PCR test. Approximately, 148 cases were tested by both the RT-qPCR and rapid tests. In this research we studied the patients who underwent both tests (PCR and rapid test) deeply and analyzed their results.

2.2 | Inclusion criteria

All the tested cases with both PCR and rapid anti-gene test during the two-month period were included in this study.

2.3 | Exclusion criteria

Cases that tested for COVID-19 using either PCR or Rapid test alone.

2.4 | Ethical approval

Ethical committee in College of Medicine, University of Baghdad approved this study (ID: 8452 in 22 Feb 2020). Their consent was taken by approving the use of the results of the tests as a data for the research.

2.5 | Rapid anti-gene test kit (SARS-CoV-2)

It was done for the patients visiting the clinic when the assessment performed using the SARS-CoV-2 Antigen Rapid Test Kit (Catalogue No. A855593), (CLINITEST®). The test was performed as per the manufacturer's instruction. All individuals were cleared of nasal secretions prior to collecting samples. A sterile swab was inserted into the nose at an angle of 90° in an extended position of neck for collecting the sample from the posterior part of the nasopharyngeal cavity, and taking five seconds and removed gently while rotating the swab. Then the swab was placed in a VTM tube, and was slopped into it five to six times before pressing. A stopper was put tightly to close the tube. It was shaken for about 15–20 s and then two drops were placed onto the specimen well of the test device given.

2.6 | RT-qPCR

Nasopharyngeal plus throat swabs were collected from suspected cases for RT-qPCR using special nylon flocked swab rods which were placed in a 3-mL VTM tube (Catalogue No. 330500C19), (Avantik VTM Viral Transport Medium NP Kit). All the samples collected in the VTM were sent to the Baghdad referral COVID-19 center, for RT-qPCR maintaining and processing protocol. All the samples collected were tested according to kits as per the protocol.

FIGURE 1 PCR test and rapid test results of the participants.

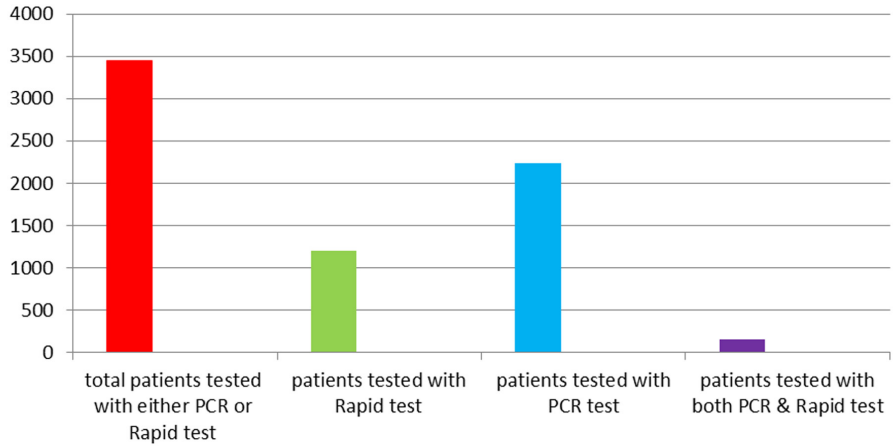

TABLE 1 RT-qPCR test and rapid anti-gene test results of the participants.

	RT-qPCR		Total
	Positive	Negative	No. (%)
Rapid anti-gene test			
Positive	11 (7.4)	41 (27.7)	52 (35.1)
Negative	18 (12.2)	78 (52.7)	96 (64.9)
Total	29 (19.6)	119 (80.4)	148

Note: Sensitivity 37.93% (20.69–57.74). Specificity 65.55% (56.28–74.02). Positive Predictive Value (*) 4.39% (2.64–7.21). Negative Predictive Value (*) 96.2% (94.88–97.2). Accuracy (*) 64.44% (56.16–72.13).

TABLE 2 Rapid anti-gene test results.

	Positive	Negative
Test	No. (%)	
IgG	47 (31.8)	101 (68.2)
IgM	18 (12.2)	130 (87.8)

TABLE 3 Rapid IgG test and RT-qPCR test results of the participants.

	Rt-qPCR		
	Positive	Negative	Total
	No. (%)	No. (%)	No. (%)
IgG			
Positive	10 (6.8)	37 (25.0)	47 (31.8)
Negative	19 (12.8)	82 (55.4)	101 (68.2)
Total	29 (19.6)	119 (80.4)	148

Note: Sensitivity 34.48% (17.94–54.33). Specificity 68.91% (59.77–77.07). Positive Predictive Value (*) 4.42% (2.55–7.54). Negative Predictive Value (*) 96.19% (94.97–97.12). Accuracy (*) 67.53% (59.35–74.99).

2.7 | Statistical analysis

The collected data was analyzed using MedCalc's Diagnostic test evaluation calculator (MedCalc Software Ltd). Results were described in the form of frequencies and percentage distribution for qualitative data. We depended upon a 2×2 contingency table for determining the sensitivity, specificity, positive predictive value, negative predictive value and accuracy.

3 | RESULTS

Three thousand four hundred forty cases were tested during the eligible period using either RT-qPCR or rapid anti-gene test, 1199 cases from the total cases were tested using just the rapid anti-gene test and 2241 cases from the total cases were tested using the Rt-qPCR test. A total of 148 cases were tested using both the RT-qPCR and rapid test (Figure 1). Twenty-nine (19.6%) of these cases had positive results for RT-qPCR and 119 (80.4%) were negative, whereas, 52 (35.1%) patients were positive to rapid anti-gene test and 96 (64.9%) of them negative, of which 11 (7.4%) were positive RT-qPCR and positive rapid anti-gene test, and 41 (27.7%) were negative RT-qPCR and positive rapid test, 18 (12.2%) were positive RT-qPCR and negative rapid test and 78 (52.7%) were negative RT-qPCR and negative rapid test, (Table 1). Depending on the COVID-19 test results, the sensitivity of the rapid test was 37.9% (95% CI 20.6%–57.7%), the specificity was 65.5% (95% CI 56.2%–74%) and the accuracy was 64.44% (95% CI 56.16%–72.13%).

Table 2 showed the percentage distribution of rapid anti-gene test. Rapid IgG test was positive in 47 (31.8) of cases, while it was negative in 101 (68.2%) of cases. Although, rapid IgM test was positive in 18 (12.2%) of cases, it was negative in 130 (87.8%) of patients.

Individual comparison of each rapid anti-gene test are listed in (Tables 3 and 4), respectively. The rapid IgG test was more sensitive than rapid IgM (Sensitivity 34.48% vs. 3.45%), but it was less specific than rapid IgM test (Specificity 68.91% vs. 85.71%). The accuracy for rapid IgG and IgM tests were 67.53% and 82.42%, respectively.

We summarized rapid anti-gene tests and RT-qPCR findings with our notes in (Table 5).

4 | DISCUSSION

The current work is a cohort hospital-based study conducted for assessment of the sensitivity and specificity of rapid anti-gene tests in comparison with Rt-qPCR (the gold standard test).

The results in this research revealed that the sensitivity of the rapid anti-gene tests was 37.9% and the specificity was 65.5%. When compared with the data of many studies conducted in other countries, we found the sensitivity and specificity to be low.[17–23] These could be explained by differences in sampling size, active preventive and control programs, and advance searching strategies in those countries in comparison to our country. The sensitivity of rapid anti-gene test ranged between 29% and 93.9%, and the specificity ranged between 80.2% (95% CI 71.1–86.7) and 100% (95% CI 98.8%–100%) according to EU/EEA and UK study.[24]

Rapid antigen test kits could be used as a screening test for ruling out COVID-19, but it has lower significance when used on asymptomatic cases, as well as in regions with a high viral load, the sensitivity reached as high as 88%.[23]

TABLE 4 Rapid IgM test and RT-qPCR test results of the participants.

	RT-qPCR		
	Positive	Negative	Total
	No. (%)	No. (%)	No. (%)
IgM			
Positive	1 (0.7)	17 (11.5)	18 (12.2)
Negative	28 (18.9)	102 (68.9)	130 (87.8)
Total	29 (19.6)	119 (80.4)	148

Note: Sensitivity 3.45% (0.09–17.76). Specificity 85.71% (78.12–91.45). Positive Predictive Value (*) 1% (0.14–6.76). Negative Predictive Value (*) 95.52% (95.07–95.93). Accuracy (*) 82.42% (75.32–88.18).

The recorded sensitivity varied worldwide range (70.0%–93.9%) and also the specificity ranged from (92.0%–100.0%), in addition, the severe infection and antigen loading have been critically determining factors to revealed such data.[23]

The sensitivity of the rapid IgM test was lower than rapid IgG test, whereas the specificity was higher. The sensitivity of Covid-Presto® test for both IgM and IgG titer were 78.4% and 92%, respectively, and the specificity for IgM was 100% for Covid-Presto®, and IgG was 92% in a France study.[25] Zandi et al.,[15] concluded that advance molecular diagnostics guidelines beside other anti-gene kits may increment a well-managed global control to decrease deaths from this pandemic.

According to the local protocol of our hospital, the probability of each case of test results are as following:

- IgG negative, IgM negative, and PCR positive (window of infection).
- When all of IgG, IgM, and PCR are positive (active phase infection).
- IgG negative but both of IgM and PCR are positive (early stage infection).
- IgM is negative but both of IgG and PCR are positive (late or recurrent stage of infection).
- IgG and PCR are negative but IgM is positive (stage of infection).
- IgG is positive but both IgM and PCR are negative (past infection and recovered).
- Both IgM and IgG are positive but PCR is negative (recovery stage).
- The entire results negative (healthy).

It is preferable to conduct diagnostic tests of COVID-19, rapid anti-gene test and RT-qPCR tests for suspected COVID-19 patients; this will give us more accurate and specific diagnostic findings.

Zandi et al.,[15] mentioned that most studies' citations involved in his systematic review used different sequences of COVID-19 ORF genes in their laboratories, and they accounted for the highest rate of prevalence of COVID-19 infectivity in RT-PCR assays.

TABLE 5 Summary of rapid IgG and IgM tests, and RT-qPCR findings.

IgG	IgM	RT-qPCR	No.	Notes
Negative	Negative	Positive	18	Patient may be in the window of infection
Positive	Positive	Positive	0	Patient may be in the active phase infection
Negative	Positive	Positive	1	Patient may be in the early stage infection
Positive	Negative	Positive	10	Patient may be in the late or recurrent stage of infection
Negative	Positive	Negative	5	Patient may be in the stage of infection, so PCR result may be false-negative
Positive	Negative	Negative	25	Patient may have had a past infection and has recovered
Positive	Positive	Negative	12	Patient may be in the recovery stage of an infection or the PCR result may be false infection
Negative	Negative	Negative	77	There is no infection

5 | CONCLUSION

We cannot consider rapid anti-gene test alone as a diagnostic method for COVID-19. We should also carry out a RT-PCR test and other investigations like imaging CT scan of chest to confirm the diagnosis. The rapid IgG test is more sensitive than rapid IgM, but it was less specific.

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None.

CONFLICT OF INTEREST STATEMENT

None.

DATA AVAILABILITY STATEMENT

Oday Taher Mohammed Al-Hashimi. (2022). The sensitivity and specificity of COVID-19 rapid anti-gene test in comparison to RT-PCR test as a gold standard test. https://doi.org/10.5281/zenodo.7491220.

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