Original Article

Agreement Between the Rapid Antigen Test for SARS-CoV-2 and the RT-qPCR Diagnostic Test

Concordancia entre la prueba de antígenos rápida para SARS-CoV-2 y la prueba diagnóstica de RT-qPCR

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Summary

Objective: to assess the agreement between the rapid antigen testing (RATs) for SARS-CoV-2 and quantitative reverse transcription polymerase chain reaction (RT-qPCR). **Methods:** analytical cross-sectional study, conducted in three medical units from January 1, 2021, to June 30, 2022, in Mexico City, Mexico. Non-probabilistic sampling was performed using data from the Online Notification System for Epidemiological Surveillance. Data analysis was performed using frequency measures, Cohen's kappa index, and maximum likelihood estimation. **Results:** Of 2173 participants with both diagnostic tests: 565 respiratory samples were concordant with a positive result (26.09% CI95% 24.25 - 27.99%), and 1229 with a negative result (56.55% CI95% 54.44 - 58.65%). The sensitivity of RAT versus RT-qPCR was estimated to be 65.17% (95%CI 61.99 - 68.33%), while the specificity was 94.10% (95%CI 92.82 - 95.38%); a positive predictive value of 88.01% (95%CI 85.23 - 90.41%), and a negative predictive value of 80.27% (95%CI 78.19 - 82.24%). The Cohen's kappa index was 0.62 (substantial agreement), and a calculated likelihood ratio of 40% at pre-test prevalence, a post-test probability of 88.3% was observed for a positive result with RAT in case of having COVID-19. **Conclusion:** The present study demonstrated substantial concordance between RAT and RT-qPCR, supporting the feasibility of using both tests. This provides clinicians with a valuable tool for informed decision making in the diagnostic context of COVID-19.

Keywords: Accuracy, COVID-19, RT-qPCR, Antigen.

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Resumen

Objetivo: estimar la concordancia de la prueba de antígenos rápida (PAR) para SARS-CoV-2 y la prueba de reacción en cadena de la polimerasa cuantitativa con transcripción inversa (RT-qPCR). **Métodos:** estudio transversal analítico, realizado en tres unidades médicas del 1 de enero de 2021 al 30 de junio de 2022 en la Ciudad de México, México. Se realizó muestreo no probabilístico utilizando los datos del Sistema de Notificación en Línea para la Vigilancia Epidemiológica. El análisis de datos se realizó con medidas de frecuencia, índice de kappa de Cohen e índice de máxima verosimilitud. **Resultados:** de 2173 participantes con ambas pruebas diagnósticas: 565 muestras respiratorias fueron concordantes con resultado positivo (26.09% IC95% 24.25 – 27.99%) y 1229 con resultado negativo (56.55% IC95% 54.44 – 58.65%). Se estimó que la sensibilidad de la PAR frente a RT-qPCR fue de 65.17% (IC95% 61.99 – 68.33%) mientras que la especificidad fue de 94.10% (IC95% 92.82 – 95.38%); un valor predictivo positivo de 88.01% (IC95% 85.23 – 90.41%) y valor predictivo negativo de 80.27% (IC95% 78.19 – 82.24%). El índice de kappa de Cohen fue de 0.62 (concordancia sustancial) y una razón de verosimilitud calculada de 40% ante una prevalencia preprueba, se observó una probabilidad posprueba del 88.3% para un resultado positivo con PAR en caso de tener la COVID-19. **Conclusión:** el presente estudio reveló una concordancia sustancial entre PAR y RT-qPCR, lo que respalda la viabilidad del uso de ambas pruebas. Esto proporciona a los clínicos una herramienta valiosa para la toma de decisiones informadas en el contexto diagnóstico de la COVID-19.

Palabras clave: precisión, COVID-19, RT-qPCR, antígeno.

Introduction

Latin America is one of the most affected regions by the disease caused by coronavirus-19 (COVID-19); eight of the ten countries with the highest mortality are located in this region.[1] In Mexico, it has been reported that at least 2.5 million inhabitants have already suffered from COVID-19 by May 2021, with a mortality rate close to 10%[2], and an average of 1428 deaths per week, with health care workers being an important risk group.[3]

To identify this disease, a reliable diagnosis is required to detect SARS-CoV-2, as the clinical manifestations can be difficult to distinguish from other respiratory infections; also, its sensitivity can change as the virus decreases its presence in tissues in parallel with the action of the immune response.[4]

At the beginning of the pandemic, the diagnosis was made by RT-qPCR assay, considered the gold standard because of its high sensitivity,[5,6] which was 95% for the original virus when performed within the first five days of infection, decreasing to values between 76-84% during days six to eight, continuing to decrease to 50% by day eighteen. For its part, the specificity of this test has been estimated at ≥99% regardless of the days of collection.[4]

However, the technical and logistical difficulties associated with RT-qPCR tests have led to the need to use other molecular techniques to facilitate their operability,[7,8] which is why the use of viral rapid antigen detection (RAT) tests has been chosen worldwide, as they are easier and cheaper to perform, and improve waiting times.[9]

RAT proved to be a suitable option for estimating the prevalence and lethality of the disease, as well as for epidemiologic surveillance, leading to the development, and marketing of several devices with different technical characteristics that led to discordant results if the tests were not performed in strict accordance with the manufacturer's instructions. The emergence of new viral variants reduced the sensitivity of the original detection tests.[10,11] Therefore, the aim of this study was to evaluate the concordance of RAT versus RT-qPCR in the context of their routine use in Mexico.

Methods

Cross-sectional analytical study conducted in three medical units of the Mexican Institute of Social Security (IMSS) (General Regional Hospital No. 1, General Regional Hospital No. 1-A, and General Hospital of the zone with Family Medicine No. 8) during the period from January 1, 2021 to June 30, 2022 in Mexico City, Mexico. Consecutive sampling was performed using all data from the Online Notification System for Epidemiologic Surveillance (SINOLAVE) during the study period. Inclusion criteria were RT-qPCR and RAT, age between 0 and 99 years, of both genders. Those records whose samples were rejected or not performed because they did not comply with the protocol for acceptance of biological samples at the Central Epidemiological Laboratory (LCE) of the IMSS were excluded. To reduce bias, those cases with RAT or RT-qPCR that were identified as having been performed in another health institution or private laboratory, or if the period was outside the limit established by the manufacturer for the use of RAT, were eliminated.

To obtain the data, the first contact physician applied the Epidemiologic Study of Viral Respiratory Disease, if

it corresponded to the operational definition in force at the time of the study, and entered the data into the SINOLAVE system, where the results of the RATs of the Medical Unit Laboratory, and RT-qPCR of the LCE were issued.

Data analysis was performed by calculating frequency measures, central tendency, and dispersion. Normality tests were performed to determine the distribution of quantitative variables. Agreement between the two tests was estimated by calculating Cohen's kappa index, where <0.00 is no agreement, 0.01-0.20 is insignificant agreement, 0.21-0.40 is moderate agreement, 0.41-0.60 is moderate agreement, 0.61-0.80 is substantial agreement, and 0.81-1.00 is near perfect agreement.[12] The maximum likelihood index was estimated[13] to compare the probabilities of having or not having COVID-19. Data were analyzed using the IBM Statistical Package for Social Sciences (SPSS) version 26.

The present study was approved by the local health research and ethics committee.

Results

A total of 39,717 records were identified in the SINOLAVE platform during the study period in the three medical units. After applying the selection criteria, 2173 participants were identified and constituted the analyzed sample. The median age was 46 years with an interquartile range (IQR) of 32-63 years, with a predominance of females (53.33%) compared to males (46.66%). The median time from symptom onset to seeking medical attention was estimated to be 3 days (Table 1).

Of the total number of cases, 81.60% were discharged due to improvement, 16.50% died, 1.90% were transferred to another hospital for further care; simultaneously, a categorization by age in tens was performed (Table 1), showing that the highest number of cases occurred between the ages of 30 and 39 years (19. 74%, 95% confidence interval [95%CI] 18.08 - 21.47%), mortality was higher in the population aged 60 to 69 years (4.29%, 95%CI 3.38 - 5.11%), and in those aged 70 to 79 years (4.14%, 95%CI 3.34 - 5.06%).

An epidemic curve was plotted (Figure 1), in which an increase in cases was observed during the winter season, with a peak at the beginning of 2022.

Regarding the most frequent symptoms in the study, headache (79.88%), cough (79.38%), attack on general condition (63.92%), fever (63.82%), and dyspnea (45.74%) predominated.

Table 1. Epidemiological Characteristics of the Participants

	Frequency	Percentage	CI 95%
Patient Management			
Hospitalization	943	43.33	41.29-45.51
Outpatient	1230	56.66	54.48-58.70
Medical Unit			
HGZMF 8	665	30.60	28.66-32.58
HGZ 1	1152	53.01	50.88-55.13
HGZ 1A	356	16.38	14.84-18.00
Gender			
Woman	1159	53.33	51.21-55.45
Man	1014	46.66	44.54-48.78
Age in Years			
0 a 9	53	2.43	1.83-3.17
10 a 19	57	2.62	1.99-3.38
20 a 29	329	15.14	13.65-16.71
30 a 39	429	19.74	18.08-21.47
40 a 49	352	16.19	14.67-17.81
50 a 59	308	14.17	12.73-15.71
60 a 69	259	11.91	10.58-13.35
70 a 79	232	10.67	9.40-12.05
80 a 89	127	5.84	4.89-6.91
90 a 99	27	1.24	0.08-1.80
	Median	**IQR**	
Age in years	46	32 - 63	
Interval IS – SA	3.00	0.00 - 7.00	

CI 95%: 95% Confidence Interval
HGZ: General Hospital of the Zone
HGZMF: General Hospital of the Zone with Family Medicine
IQR: Interquartile range
IS - SA: Onset of symptoms and request for care

Figure 1. Epidemic Curve. Registered cases of viral respiratory disease from January 1, 2021 to June 30, 2022

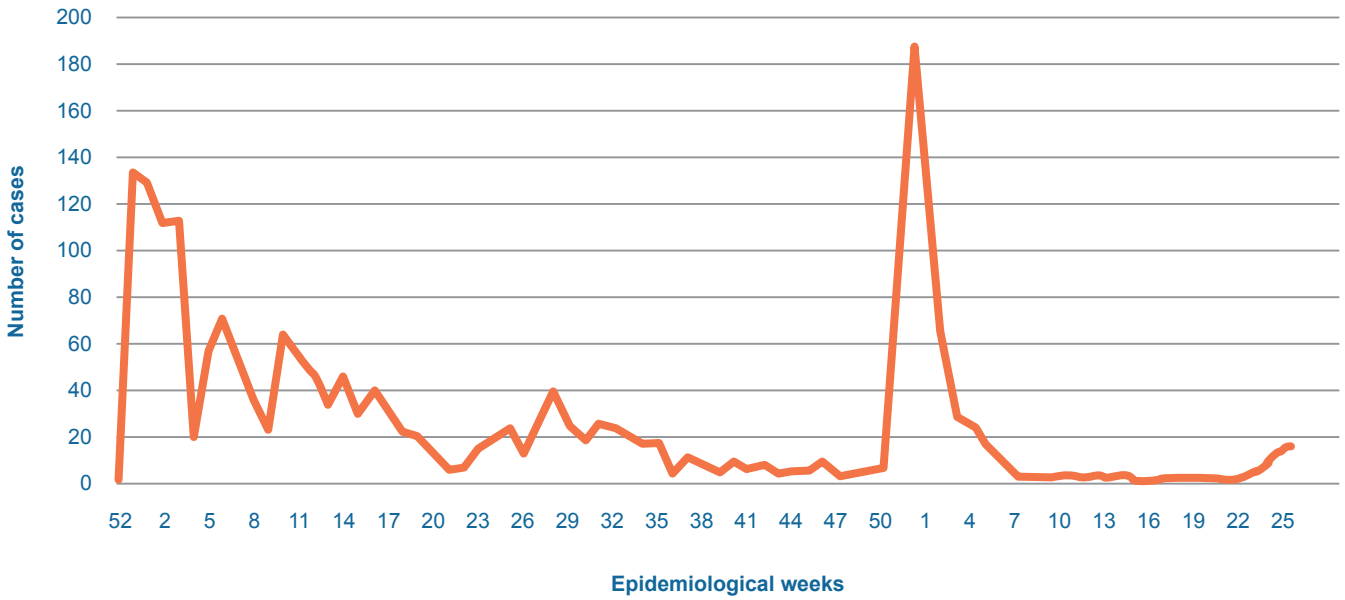

Table 2 shows the contingency pooling the results of both diagnostic tests for the 2173 participants. A total of 565 respiratory specimens were concordant for a positive result (26.09% CI95% 24.25 - 27.99%), and 1229 were concordant for a negative result (56.55% CI95% 54.44 - 58.65%).

On the other hand, the sensitivity of RAT versus RT-qPCR was 65.17% (95%CI 61.99 - 68.33%), while the specificity was 94.10% (95%CI 92.82 - 95.38%).

The positive predictive value was 88.01% (95%CI 85.23 - 90.41%), and the negative predictive value was 80.27% (95%CI 78.19 - 82.24%). Cohen's kappa index was used to assess concordance and was reported as 0.62 (substantial concordance).

According to the likelihood ratio calculated at a pretest prevalence of 40%, the post-test probability of a positive result with RAT using COVID-19 was 88.3%. Table 3 shows the results of the diagnostic performance estimates.

Finally, the secondary analysis was performed by day (Table 4), in which it was observed that when RAT is performed between the first and fourth day after symptom onset, there is substantial agreement (0.62-0.68), with a sensitivity ranging from 65.18-70. 41%. On the other hand, when RAT is performed on the same day of symptom onset or from the fifth day, the results for these estimates decrease.

Table 2. Contingency table for RT-qPCR and RAT results

	RT-qPCR result		
RAT result	positive	negative	total
positive	565 (TP)	77 (FP)	642
negative	302 (FN)	1229 (TN)	1531
total	867	1306	2173

RT-qPCR: Reverse Transcriptase Chain Reaction Test
RAT: Rapid Antigenic Test
TP: True Positive
TN: True Negative

Discussion

Current evidence suggests that there is no biological gender difference in the development of COVID-19,14 however, this study showed that women were more likely to have acquired the disease. Similar to national statistics, the largest age group was observed between 30 and 39 years, and most cases were resolved on an outpatient basis with improvement.[15] In addition, the majority of deaths from COVID-19 occurred in older adults.[16]

Regarding the emergence of new variants of SARS-COV-2, Omicron (B.1.1.159) was detected in early November 2021, which was highly transmissible and was reflected in an increase in cases worldwide,[17] consistent with what was observed in Figure 1.

The main symptoms in patients with COVID-19 are fever, cough and dyspnea,[18-20] which may be indistinguishable from those caused by other viral infections similar to the manifestations observed in this study. Given this sce-

Table 3. Estimates of the RAT versus RT-qPCR Performance

Measure	Estimate	95% CI
Sensitivity	65.17%	61.99 - 68.33%
Specificity	94.10%	92.82 - 95.38%
Positive predictive value	88.01%	85.23 - 95.38%
Negative Predictive Value	80.27%	78.19 - 82.24%
Positive Likelihood Ratio	11.10	8.85 - 14.00
Negative Likelihood Ratio	0.37	0.34 - 0.41
Cohen's Kappa	0.62	0.57 - 0.66

95% CI: 95% Confidence Interval

Table 4. Estimates of RAT Versus RT-gPCR Performance by Day of Performance Since Symptoms Onset

Days	n	%	Sen	Spe	PPV	NPV	Kappa
0	250	11.50	58.57%	93.89%	78.85%	85.35%	0.569
1	377	17.30	65.18%	96.98%	90.12%	86.82%	0.676
2	369	17.00	70.00%	93.72%	85.85%	85.17%	0.665
3	389	17.90	70.41%	93.64%	89.47%	80.47%	0.657
4	260	12.00	65.69%	93.67%	87.01%	80.87%	0.621
5	249	11.50	63.36%	94.92%	93.26%	70.00%	0.573
6	172	7.90	60.00%	88.89%	88.24%	61.54%	0.460
7	107	4.90	58.49%	90.74%	86.11%	69.01%	0.494

Sen: Sensitivity, Spe: Specificity, PPV: Positive Predictive Value, NPV: Negative Predictive Value

nario, there is a need for diagnostic tests capable of identifying specific pathogens that can be widely used from a public health perspective.

It has been documented that RATs with higher sensitivity and specificity can match RT-qPCR assays for detection of infection. Similarly, the sensitivity of RATs has been found to range from 45% to 97%, however, this is influenced by different producing laboratories, clinical characteristics of patients, severity of disease, site of test collection, handling and reading time.[6,21] This study evaluated commercial RAT devices purchased by the IMSS, regardless of their manufacturer, for the detection and control of COVID-19 and found a sensitivity of 65.17%.

A systematic review showed sensitivity and specificity for RAT of 70% (95%CI 69-71%), and 98% (95%CI 98-99%), respectively,[21] while another study showed sensitivity of 93.9% and specificity of 100% with a Kappa index of 0.9.[22] A study of diagnostic accuracy showed sensitivity of 87.6%, and specificity of 99.9%;[23] these results may be directly influenced by sample size in a period of high disease incidence and suggestive symptomatology during the first week of illness. In this context, a meta-analysis of eleven studies showed a sensitivity of 86% (95%CI 84-88%), and specificity of 99% (95%CI 98-99%), demonstrating that the use of RAT is a reliable alternative for the detection of SARS-CoV-2 infection.[24]

On the other hand, a study published in India showed a sensitivity of 61% and a specificity of 94.4%, results comparable to those obtained in our study (Table 3). The main difference is that the Indian study included asymptomatic patients in its analysis.

Furthermore, it has been reported that the probability of transmission is higher during the first week due to the increase in viral load, which coincides with the onset of symptoms in infected patients.[23,26] Subsequently, the sensitivity of the tests decreases due to the decrease in viral load; this decrease in sensitivity can be seen in Table 4.

As there are no specific clinical features to differentiate COVID-19 from other viral respiratory diseases, asymptomatic participants were not included in this study.

Limitations include the use of a secondary data source that was not designed to meet the objectives of the study, since its use is adapted to the context of clinical and epidemiologic follow-up, but it describes an important part of the cases registered during the study period.

Conclusion

The current study showed a sensitivity of 65.17% and specificity of 94.10% for RAT versus RT-qPCR, demonstrating substantial agreement. These results support the utility of RAT as an acceptable and viable option given the cost and time to obtain results. This provides clinicians with a valuable decision support tool for the diagnosis of COVID-19.

Authors Contribution

A B-P: conceptualization, development, writing, analysis, and discussion of results; I C-O: conceptualization, development, and writing; C B-G: development, writing, and analysis; O M-G: development, writing, and discussion of results. All authors agree to the publication of this paper.

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Conflicts of interest

The authors declare not having competing interests.

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