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Brief Report

Comparative Performance of a Rapid SARS-CoV-2 Antigen Test with RT-PCR for the Diagnosis of COVID-19

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Abstract

Background: The aim of this study was to estimate the diagnostic precision of the rapid COVID-19 antigen test DyonCovid-Ag compared to the gold standard method Reverse Transcription quantitative Polymerase Chain Reaction (RT-qPCR) for the diagnosis of SARS-CoV-2 infection. **Methods:** This prospective cohort study examined samples from non-hospitalized adults and children with possible SARS-CoV-2 infection from 01/2021–12/2021. The samples were double tested using the rapid SARS-CoV-2 antigen test DyonCovid-Ag and an RT-qPCR for SARS-CoV-2. Demographic data and clinical symptoms were also collected. **Results:** A total of 782 individuals with median age 36.6 years (IQR: 28-48) were included in this study. The positivity for SARS-CoV-2 was 128/782 (16.4%) with RT-qPCR and 123/782 (15.7%) with RAT. The concordance of positive samples between two methods was high (123/128, 96.1%), with only five false negative but no false positive results. The sensitivity and specificity of the RAT were estimated at 96.1% (95%CI: 91.1-98.7%) and 100% (95%CI: 99.4-100.0%), respectively. Accuracy was estimated at 99.4% (95%CI: 98.5-99.8%). **Conclusion:** DyonCovid-Ag RAT was highly sensitive and specific and could facilitate timely diagnosis in point-of-care settings.

Keywords: COVID-19; SARS-CoV-2; Rapid antigen test; Reverse Transcription quantitative Polymerase Chain Reaction (RT-qPCR).

Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) continues to spread worldwide, increasing disease incidence, reinfections and breakthrough infections. COVID-19 cannot be differentiated from other viral respiratory infections based on specific clinical criteria [1]. There are several diagnostic approaches in the acute phase of infection. The gold standard diagnostic method is the Reverse Transcription quantitative Polymerase Chain Reaction (RT-qPCR) which usually consists of several procedural steps that make it time consuming [2,3]. Although there are close RT-qPCR systems that minimize hands-on time, the minimum exam time is about one hour [4]. Rapid diagnosis is crucial for patient management, contributing to the immediate treatment and good prognosis of patients, especially those with comorbidities. Thus, rapid antigen tests (RAT) were soon produced. RATs are practical, handy, and economical [5].

The aim of this study was to estimate the diagnostic accuracy of RAT DyonCovid-Ag compared to the gold standard method RT-qPCR for the diagnosis of SARS-CoV-2 infection.

Materials and methods

This was a prospective cohort study involving adults and children with possible SARS-CoV-2 infection from 01/2021-12/2021. Candidates for participating in the study were individuals of any age with or without clinical symptoms (upper respiratory tract infection symptoms, fever or other), individuals who had been in contact with a COVID-19 case in the previous two or more days and individuals who tested for travel and work issues.

The participants for SARS-CoV-2 testing visited one of the following three centers: "Aghia Sophia" Children's Hospital, Athens, Greece, the polyclinic "Diagnostiki Athinon" in Athens, Greece and the polyclinic "Advanced Medical Services (AMS)" from Athens and Mykonos in Cyclades of Aegean Sea, Greece. Two nasopharyngeal swabs were collected from each subject. One swab for RAT testing and the other for RT-qPCR (Figure 1). RATs were directly performed after sampling at each center, while RT-qPCRs were conducted at Infectious Diseases Laboratory of the National and Kapodistrian University of Athens. Participants were tested with both tests by qualified personnel twice a month. Demographic data and clinical symptoms were also collected.

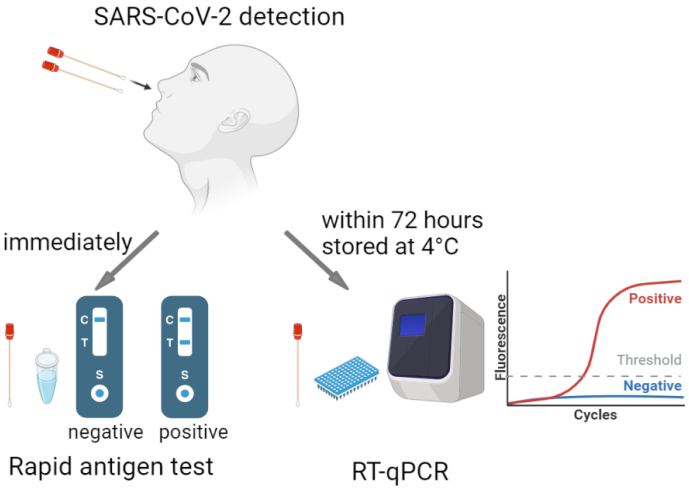

Figure 1: Study methodology. Two nasopharyngeal swabs of each participant were collected to double-test for SARS-CoV-2 infection. One swab was tested using a rapid SARS-CoV-2 antigen test and the other using RT-qPCR.

The study was carried out according to with the Declaration of Helsinki, and the study protocol was approved by the scientific and bioethics committee of "Aghia Sophia" Children's Hospital (No: 2794). Informed consent was obtained from all participants.

Viral genome isolation was performed using the MagnaPure Compact Nucleic Acid Isolation kit I (Roche Diagnostics, Basel, Switzerland) on the MagNA Pure Compact instrument. For the one-way RT-qPCR, the ARGENE SARS-CoV-2 R-Gene kit (Biomerieux, Craponne, France) targeting the nucleocapsid (N), RNA-dependent RNA polymerase (RdRp) and envelope (E) SARS-CoV-2 genes was used on the LightCycler 480 II system (Roche Diagnostics, Basel, Switzerland). When the E gene and the N or/and the RdRp genes had Ct (cycle threshold) ≤ 34, the sample was considered positive.

The RAT DyonCovid-Ag (DyonMed, ATTIKA, Greece), that was used, is an immunochromatographic assay that detects the SARS-CoV-2 nucleocapsid protein. Buffer solution, swabs and tubes were included in the kit. The results were available in 15 minutes and positive was the test with two colored bands, one in control (C) and one in test (T) positions (Figure 1).

Statistical analysis was performed using STATA (Stata Corp.) and p-value < 0.05 was considered statistically significant. The data are expressed as percentages (%), mean and standard deviation (SD) or median and interquartile range (IQR) depending on the variable and the normality. Sensitivity and Cohen's K statistic were calculated with 95% Clopper-Pearson confidence intervals. Pearson's Chi-squared was performed for categorical variables and the t-test for continuous variables.

Results

A total of 782 adults and children with possible SARS-CoV-2 infection from 01/2021–12/2021 were included in the study. The median age of 782 participants was 36.6 years (IQR: 28-48 and range: 3-92 years) and 468/782 (59.8%) were males. Divided into age groups, 39/782 (5%) were 0.5-18 years, 225/782 (28.8%) were 19-30 years, 354/782 (45.3%) were 31-50 years and 164/782 (21%) were ≥51 years. Regarding geographical location, 515/782 (65.8%) were from Athens and 267/782 (34.2%) were from the Aegean islands.

Among the 782 participants, 128/782 (16.4%) detected SARS-CoV-2 positive with RT-qPCR (median Ct=20, IQR: 16-25). The viral load distribution of positive samples detected with RT-qPCR was 24.2% (31/128) with Ct ≤ 15, 45.3% (58/128) with Ct = 16-24 and 30.5% (39/128) with Ct = 25-34. Using RAT, 123/782 (15.7%) samples were SARS-CoV-2 positive (median time of positive result was one minute, IQR: 0.9-1.1). The concordance of the SARS-CoV-2 positive samples was 123/128 (96.1%). The median age of 128 individuals with SARS-CoV-2 infection detected positive with RT-qPCR was 32.5 (IQR: 26-47.8) years old. The median age of 123 individuals who were positive for SARS-CoV-2 with RAT was 31 years (IQR: 25-46).

Divided into age groups, the estimated positivity with both

methods was 35.9% (14/39) in 0.5-18 years, 20.4% (46/225) in 19-30 years, 11.0% (39/354) in 31-50 years and 14.6% (24/164) in ≥51 years. There were 3/354 (0.9%) of participants 31-50 years and 2/164 (1.3%) of participants ≥51 years, who were negative with RAT but positive with RT-qPCR.

Symptomatic were 104/128 (81.3%) of individuals with SARS-CoV-2 positive RT-qPCR. The most frequent symptom at sampling was cough (43%) followed by headache (42%), myalgias (41%), sinus congestion (36%), malaise (30%), pharyngitis (28%), fevers/chills (27%), anosmia (23%), ageusia (23%) and rhinorrhea (21%).

The sensitivity and specificity of RAT was estimated at 96.1% (95% CI: 91.1 - 98.7%) and 100% (95% CI: 99.4 - 100.0%), respectively. Five false-negative and none false-positive samples were found using RAT (Table 1). Positive and negative likelihood ratios were estimated at 0.04 (95% CI: 0.02 - 0.09). Positive and negative predictive values were estimated at 100.0% (95% CI: 99.4 - 100.0%) and 99.2% (95% CI: 98.2 - 99.7%), respectively. The accuracy between RAT and RT-qPCR was estimated at 99.4% (95% CI: 98.5 - 99.8%). Antigen test positive samples had lower Ct values on RT-qPCR testing than antigen test negative samples ($p < 0.001$). All samples with a Ct value of ≥ 33 were negative on the RAT.

Table 1: Comparison of Reverse Transcription quantitative Polymerase Chain Reaction (RT-qPCR) and rapid antigen test for diagnosis of SARS-CoV-2 infection in 782 individuals.

		Antigen test		Total
		Positive	Negative	
RT-qPCR	Positive	123	0	123
	Negative	5	654	659
Total		128	654	782

Note: Sensitivity = 96.1% (95% CI: 91.1 - 98.7%); Specificity = 100% (95% CI: 99.4 - 100.0%); Positive predictive value = 100.0% (95% CI: 99.4 – 100.0%); Negative predictive value = 99.2% (95% CI: 98.2 - 99.7%); Accuracy = 99.4% (95% CI: 98.5 - 99.8%).

Discussion

In this study, the diagnostic accuracy of the rapid SARS-CoV-2 antigen test, DyonCovid-Ag, was evaluated in comparison with the gold standard RT-qPCR method in samples from non-hospitalized adults and children with possible SARS-CoV-2 infection. DyonCovid-Ag SARS-CoV-2 RAT was highly sensitive and specific, and its use in point-of-care settings will facilitate a timely diagnosis.

Although there are several different studies investigating the accuracy of rapid antigen and point-of-care tests for the diagnosis of COVID-19, there are no other studies evaluating the accuracy of the DyonCovid-Ag rapid test. In a study that included many asymptomatic participants tested in 2020, the efficacy of the RAT Standard Q COVID-19 Ag detection kit, compared to RT-PCR was found approximately 76% and the sensitivity was low (63%) although the specificity was high (100%) [6]. In another study involving participants also tested with CLINITEST® and RT-PCR, sensitivity and specificity were very low at 37.93% and 65.55%, respectively, and the accuracy did not exceed 64.4% [7]. Homza et al. studied five different SARS-CoV-2 RATs in more than 1,000 participants, but sensitivity did not exceed 76% while specificity (97%) was satisfying [8].

Other studies to evaluate the Coris bioconcept COVID-19 ag respi-strip test in > 400 symptomatic adults and their asymptomatic contacts, revealed 72% sensitivity, 99% specificity and 88.6% accuracy [9]. Sabat et al. studied the accuracy of Zydus Cadila RAT for SARS-CoV-2 detection and found 75% sensitivity and 99% specificity. In this study also noticed that 60% of false-negative results belong to asymptomatic participants [10]. Most of the tests are characterized by high specificity while sensitivity seems to vary. On the contrary, the Panbio COVID-19 Ag RAT showed high sensitivity (94.3%) and very low specificity (39.7%) [11].

Despite the high number of rapid tests whose evaluation was published during the last three years, only a few were evaluated through a prospective cohort of tested patients [12]. In the present study we prospectively evaluated the rapid antigen test DyonCovid-Ag compared to an established RT-qPCR method and as it was highly sensitive and specific, could facilitate timely diagnosis in point-of-care settings.

Conclusion

Three years after the emergence of SARS-CoV-2 and the beginning of the COVID-19 pandemic, the circulation of new variants of interest of the virus and breakthrough infections continue to occur. So far, there are many rapid tests to diagnose SARS-CoV-2 infection, however not all of them are characterized by high sensitivity and specificity. Therefore, there is a need for a rapid test with high diagnostic accuracy. In this study, a novel RAT was described which could facilitate timely diagnosis in point-of-care settings.

Declarations

Research funding: The antigen tests DyonCovid-Ag were offered by the company DyonMed SA.

Conflict of Interest: Authors state no conflict of interest.

Informed consent: Informed consent was obtained from all individuals included in this study.

Author contributions: Conceptualization: Athanasios Michos and Vasiliki Syriopoulou; Methodology: Elizabeth Barbara Tatsi, Syridon Mparmpas and Vasileios Sideris; Formal analysis and investigation: Elizabeth Barbara Tatsi, Syridon Mparmpas and Vasileios Sideris; Writing - original draft preparation: Elizabeth Barbara Tatsi and Filippos Filippatos; Writing - review and editing: Athanasios Michos and Vasiliki Syriopoulou; Supervision: Athanasios Michos and Vasiliki Syriopoulou. All authors reviewed and approved the final manuscript.

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