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Short research communication

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Abstract

Background: Early and accurate diagnosis is crucial for preventing the spread of SARS-CoV-2 infection. The rapid antigen test was developed for testing infection, and it was necessary to assess its performance before widespread use in Tunisia.

Aim: To evaluate the effectiveness of a rapid antigen test for the detection of SARS-CoV-2 in nasopharyngeal swabs in Tunisia.

Methods: Nasopharyngeal samples were taken from COVID-19 suspected cases between October and December 2020 and tested using the Standard Q COVID-19 Ag test (SD-Biosensor, Republic of Korea) and real-time reverse transcription polymerase chain reaction (RT PCR).

Results: Overall, 4539 patients were tested. Of the total study population (N = 4539), 82.5% of positive samples remained positive with the rapid antigen test, while 20.2% (470/2321) of samples that were negative with rapid antigen test were confirmed positive with RT-PCR, giving a negative predictive value of 79.8% for the rapid antigen test. The sensitivity and negative predictive value of the rapid antigen test were 70.2% and 65.8%, respectively. These results improved to 96.4% and 92.8%, respectively, when considering the cycle threshold value by RT-PCR below 25.

Conclusion: Although the rapid antigen test was less sensitive than RT-PCR, its ability to rapidly detect individuals with high viral loads makes it suitable for use during an epidemic.

Keywords: COVID-19, SARS-CoV-2, rapid antigen test, RT-PCR, analytical performance

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Introduction

SARS-CoV-2 was first reported in December 2019 and it spread rapidly worldwide, causing a global pandemic (1, 2). Currently, transmission of the virus has decreased but an outbreak could appear in any country at any time. Early and accurate diagnosis is crucial for preventing the spread of the disease. The current gold standard for the detection of SARS-CoV-2 RNA is reverse transcription polymerase chain reaction (RT-PCR) (3). Despite the excellent performance of RT-PCR, many hours of handling by trained technicians are required to obtain reliable results. In many countries, access to this expensive method is difficult, and a PCR-only-based testing strategy cannot be applied. The need to develop reliable, easy-to-perform, less expensive and faster diagnostic tools emerged as a top priority. Among these tools, rapid antigen tests was developed and several are now commercially available, although reported performance of these tests has varied among studies (4). The Microbiology Laboratory of Habib Bourguiba University Hospital, Sfax, Tunisia, was one of the places that had the capability to carry out RT-PCR for diagnosis of SARS-COV-2. In September 2020, an upsurge in COVID-19 cases was observed in Tunisia. To limit the spread of the disease, the Tunisian health authorities introduced the rapid antigen test (STANDARD Q COVID-19 Ag), and recommended an assessment of its performance before widespread use.

The objective of this study was to evaluate the performance of the rapid antigen test provided by the Tunisian Ministry of Health for the diagnosis of SARS-CoV-2 infection at the Microbiology Laboratory of Habib Bourguiba University Hospital, Sfax, Tunisia.

Methods

A prospective study was conducted in October–December 2020 at Habib Bourguiba Hospital in Sfax, Tunisia. First, to assess the analytical performance of the SARS-CoV-2 rapid antigen test, a group of 74 symptomatic patients with suspected COVID-19 who presented at the primary care unit in late October 2020, had two simultaneous nasopharyngeal swabs taken from them. The first swab was tested onsite by the rapid antigen test, and the second swab was sent to the microbiology laboratory for confirmation by RT-PCR. In a second step, during November–December 2020, the rapid antigen test was used on nasopharyngeal swabs from 4465 patients. All negative samples were further confirmed using RT-PCR.

The rapid antigen test used in this study was the STANDARD Q COVID-19 Ag test (SD BIOSENSOR, Republic of Korea). It is a rapid chromatographic immunoassay for the detection of SARS-CoV-2 nucleocapsid antigen in nasopharyngeal swabs within 15–20 minutes, with a lower limit of detection of 5.103.2 TCID50/ml for swabs stored in viral transport medium. For SARS□CoV□2 detection by real-time RT□PCR, viral RNA was extracted in an automated extraction platform, and tested for SARS-CoV-2 using the COVID-19 Genesig Real-Time PCR (Primerdesign Ltd., Chandler's Ford, UK). This targets the RNA-dependent RNA polymerase gene in the open reading frame ORF1ab. The reverse transcription and amplification were performed using the Applied Biosystems QuantStudio 5 Real-Time PCR System (Life

Technologies Holdings, Singapore). Samples showing a cycle threshold (Ct) value 30 no longer contagious (5).

All reagents were provided by the Tunisian Ministry of Health.

Data were analysed using SPSS version 20.0. Rapid antigen test performance was assessed through determination of sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) using the RT-PCR results and Ct values as references. $P \leq 0.05$ was considered significant.

Oral informed consent was obtained from all included patients.

Results

We tested 4539 samples. Most samples (98.1%) were taken during the first week from the onset of clinical symptoms. The mean duration between symptom onset and sampling was 4 (1–20) days.

Among the first 74 patients tested, the rapid antigen test was positive in 33; all of whom were confirmed positive by RT-PCR. Fourteen of the 41 samples (34.1%) that were negative with the rapid antigen test were positive with RT-PCR. Detection rates of SARS-CoV-2 with rapid antigen test and RT-PCR were 44.6% (33/74) and 63.5% (47/74), respectively. The median Ct values for the RT-PCR in patients with positive and negative rapid antigen tests were 20.1 (14.7–38.3) and 34.4 (23.2–37.8), respectively (P

Given the excellent specificity of the rapid antigen test, further testing by RT-PCR was performed only for negative samples. Among 4465 patients enrolled in the second part of the study, 2280 had negative rapid antigen test but 456 (20%) were positive for SARS-CoV-2 RNA with the RT-PCR.

Among the whole study population (N=4539), 82.51% of the total positive samples were positive when we used the rapid antigen test (2218/2688). Among 2321 samples that were negative with rapid antigen test, 470 (20.2%) were confirmed positive for SARS-CoV-2 RNA with RT-PCR. This gave an NPV of 79.8% for the rapid antigen test. The mean Ct value in these patients was 33.6. Ct value was ≤ 25, 25–30 and >30 in 3.2%, 14.25% and 82.55% of cases.

During the study period, the positivity rate was 45.2% among the 3701 rapid antigen tests performed during the first week of illness and 37.2% among the 78 performed after this date (P = 0.19).

Discussion

Most antigen tests detect nucleocapsid protein of SARS-CoV-2, which is a structural protein that displays less variation than the spike protein. Although the rapid antigen test in our study was used during circulation of the original Wuhan strain of SARS-CoV-2, many studies have demonstrated the effectiveness of rapid antigen tests, including STANDARD Q COVID-19 Ag, for the detection of SARS-CoV-2 variants (6, 7). The STANDARD Q COVID-19 Ag test is one of the tests recommended by WHO for emergency use to diagnose SARS-CoV-2 infection (8).

The main finding of our study was the ability of the STANDARD Q COVID-19 Ag test to achieve early diagnosis of SARS-CoV-2 infection. This could be because the targeted nucleocapsid protein can be detected up to 1 day before onset of clinical symptoms and is therefore one of the best markers for early diagnosis of SARS-CoV-2 infection (9).

Different results have been obtained when comparing the performance of currently available rapid antigen tests and RT-PCR (10). A systematic review and meta-analysis published by Lee et al. in 2021 focused on 24 studies including 14 188 patients (11). The overall pooled sensitivity and specificity of different rapid antigen tests for the diagnosis of SARS-CoV-2 infection were 68% and 99%, respectively. The sensitivity and specificity of the STANDARD Q COVID-19 Ag test in our study were 70.2% and 100%, respectively, although the sensitivity of the test was markedly lower than that reported by the manufacturers (96.52%). However, we have demonstrated that the sensitivity improved to 94.1% and 96.4% when Ct values were reduced to ≤ 30 and ≤ 25, respectively. These results agree with the above systematic review and meta-analysis, which showed that the pooled sensitivity of rapid antigen tests was 84% for Ct values ≤ 30, and increased to 94% when the Ct values were ≤ 25 (11). Ct reflects the viral load in the initial specimen, which depends on the infection status of the patients (severity of illness, time of symptom onset, etc.). Ct ≤ 25 corresponds to a high viral load of > 106 genomic virus copies/mL (12). This situation usually appears in the early symptomatic phase of the infection (within the first 5–7 days) (4, 13, 14). More than 5–7 days after the onset of symptoms, patients are more likely to have lower viral loads, and the likelihood of false-negative results with rapid antigen tests is higher. In the latter meta-analysis, the pooled sensitivity of rapid antigen tests was 87% in patients tested within 5 days after symptom onset and 73% after 5 days. Similar results were found in other studies (15, 16). The exact period after symptom onset for use is not mentioned by the manufacturer of the STANDARD Q COVID-19 Ag test but in our study, the mean time course between symptom onset and sampling was 4 days.

The overall sensitivity of the STANDARD Q COVID-19 Ag test was inferior to that of the RT-PCR but the former has undoubtedly contributed to the detection of about half of all confirmed COVID-19 cases, facilitating patient management, decision-making and outbreak surveillance in our country.

The main limitation of our study was the absence of asymptomatic individuals among the study population, which could have affected the sensitivity of the rapid antigen test.

Conclusion

The STANDARD Q COVID-19 Ag test is less sensitive than RT-PCR. However, its ability to rapidly detect individuals with high viral loads makes it suitable for responding to the increased demand for diagnosis of SARS-CoV-2 infection during an epidemic. We recommend that all negative results from the rapid antigen test should be confirmed by RT-PCR. In areas where access to RT-PCRs is limited, rapid antigen tests, such as the STANDARD Q COVID-19 Ag test, could be valuable for SARS-CoV-2 diagnosis, which potentially contributes to limiting the spread of the virus.

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Competing interests: None declared.

Fiabilité du test de détection antigénique rapide pour le diagnostic du SARS-CoV-2 en Tunisie

Résumé

Contexte : Un diagnostic précoce et exact est essentiel pour prévenir la propagation de l'infection à SARS-CoV-2. Le test de détection antigénique rapide a été mis au point pour dépister l'infection, et il était nécessaire d'évaluer ses performances avant de l'utiliser à grande échelle en Tunisie.

Objectif : Évaluer l'efficacité d'un test antigénique rapide pour la détection du SARS-CoV-2 dans les prélèvements nasopharyngés en Tunisie.

WHO EMRO | Reliability of the rapid antigen test for diagnosis of SARS-CoV-2 in Tunisia

Méthodes : Des échantillons nasopharyngés ont été prélevés chez des cas suspectés de COVID-19 entre octobre et décembre 2020, et testés à l'aide du test standard Q de détection antigénique de la COVID-19 (SD-Biosensor, République de Corée) et de la réaction en chaîne par polymérase en temps réel après transcription inverse (RT-PCR).

Résultats : Au total, 4539 patients ont été dépistés. Sur l'ensemble de la population étudiée (N = 4539), 82,5 % des échantillons positifs sont restés positifs avec le test antigénique rapide, tandis que 20,2 % (470/2321) des échantillons négatifs avec ce test rapide se sont révélés positifs lors de la RT-PCR, donnant ainsi une valeur prédictive négative de 79,8 %. La sensibilité et la valeur prédictive négative de ce test étaient de 70,2 % et 65,8 %, respectivement. Ces résultats sont passés à 96,4 % et 92,8 %, respectivement, lorsque la valeur seuil du cycle de la RT-PCR est inférieure à 25.

Conclusion : Bien que le test de détection antigénique rapide soit moins sensible que la RT-PCR, sa capacité à détecter rapidement les individus ayant une charge virale élevée permet de l'utiliser pendant une épidémie.

موثوقية اختبار المستضدات السريع لتشخيص فيروس كورونا - سارس-2

امال شطورو . سبا القرقوري . عبد النور النصري . عواطف تقتق . فهمي السماوي . الفة شقرون . نور
الدين الرقيق . عدنان الحمامي . لمياء الفقي بالراجح . هالة الكراي

الخلاصة

: التشخيص المبكر والدقيق أمر بالغ الأهمية لمنع انتشار عدوى فيروسالخلفية
كورونا - سارس-2. صمم " اختبار المستضدات السريع " لاختبار العدوى، وكان من الضروري تقييم
أدائه قبل استخدامه على نطاق واسع في تونس .

: هدفت هذه الدراسة الى تقييم فعالية " الاختبار السريع للمستضدات " للكشف عن فيروسالهدف
كورونا - سارس-2 في المسحات الأنفية البلعومية في تونس .

: أُخذت عينات أنفية بلعومية من الحالات المشتبه في إصابتها بكوفيد -19 فيطرق البحث
الفترة بين أكتوبر / تشرين الأول وديسمبر / كانون الأول 2020 ، واختُبرت باستخدام

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WHO EMRO | Reliability of the rapid antigen test for diagnosis of SARS-CoV-2 in Tunisia

اختبار Q القياسي للكشف عن المستضدات الحيوية 19-□□□□□□ (BIOSENSOR-SD ، جمهورية
كوريا) و" التناسخ العكسي لتفاعل البوليميراز المتسلسل " في الوقت الحقيقي (PCR-RT).

: بوجه عام، خضع 4539 مريضًا للاختبار . وتبيَّن أن 82.51% من إجمالي العيناتالنتائ **ج**
الإيجابية التي اختُبرت باستخدام " اختبار المستضدات السريع " أو " التناسخ العكسي
لتفاعل البوليميراز المتسلسل " إيجابيًّا مع " اختبار المستضدات السريع ". وبلغت
الحساسية والقيمة التنبؤية السلبية " لاختبار المستضدات السريع " 70.2% و65.8% على
التوالي . وتحسنت هذه النتائج إلى 96.4% و92.8% ، على التوالي، عند النظر في قيمة عتبة
الدورة باستخدام " التناسخ العكسي لتفاعل البوليميراز المتسلسل " دون 25.

: على الرغم من أن " اختبار المستضدات السريع " كان أقل حساسية من " التناسخالاستنتاجات
العكسي لتفاعل البوليميراز المتسلسل " ، فإن قدرته على الكشف السريع عن الأفراد الذين
يحملون كميات فيروسية عالية تجعله مناسبًا للاستخدام في أثناء الوباء
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