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Research Article

Evaluation of a Rapid Serological Test for Covid-19 in Workers at a University Dental Hospital in Argentina

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Abstract

Introduction: The aim of the present study was to evaluate the diagnostic accuracy of a rapid test to determine SARS-CoV-2 infection in a population of workers who provided services during the COVID-19 pandemic at a University Dental Hospital.

Materials and Methods: Diagnostic accuracy was studied by comparing a commercial rapid test (PambioTM COVID 19 IgG/IgM rapid test device. ABBOTT®) to a blood test for enzyme-linked immunosorbent assays (ELISA test) as the gold standard in 284 workers at the Dental Hospital at the Buenos Aires University Dental School during the COVID-19 pandemic.

Results: Rapid test sensitivity was 0.44 (CI95: 0.14 to 0.79) and specificity was more than double (0.89; CI95: 0.85 to 0.93). The Positive predictive value was 0.12 (CI95: 0.03 to 0.27), but the negative predictive value was much higher (0.98; CI95: 0.95 to 0.99). The positive and negative likelihood ratios were 4.07 (CI95: 1.82 to 9.11) and 0.62 (CI95: 0.35 to 1.12), respectively.

Conclusion: Although it could be used for monitoring previous exposure to COVID-19 in dental health care workers, it should only be used in environments with inadequate access to more complex diagnostic tools. This method should not be used as the sole basis for treatment or other management decisions.

Keywords: *COVID-19 Pandemic; SARS-Cov2 Infection; Coronavirus; SARS-Cov-2 Rapid Test; Immunochromatographic Strip; COVID-19 Prevalence*

Introduction

A new infectious disease produced by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was detected in December 2019 in Wuhan, Hubei Province, China [1]. On March 11, 2020, the WHO declared it a global pandemic and it became a public health emergency of international concern.

Coronavirus disease-2019 (COVID-19) can be diagnosed according to a combination of epidemiological data, clinical symptoms and laboratory tests [2]. However, clinical presentation is highly variable. There are asymptomatic patients, who pose a problem at epidemiological level due to their ability to transmit the disease unperceived, and paucisymptomatic patients who have only very mild symptoms. Therefore, expansion of the testing capacity for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is important to mitigate the pandemic of coronavirus disease-2019 (COVID-19) caused by this virus.

Viral culture and real-time reverse transcription polymerase chain reaction (RT-qPCR) are the gold standards for diagnosis of

SARS-CoV-2 infection. However, it may take hours or days to secure the results of these procedures. Moreover, they require specific materials and trained personnel to take, transport and prepare the samples.

COVID-19 infection can also be detected indirectly by measuring the host's immune response to infection by SARS-CoV-2. Diagnosis by serology is especially important for patients with mild to moderate disease, who may come forward late, after the first 2 weeks since the beginning of the disease. It is also important for identifying asymptomatic individuals who have had the disease. The presence of neutralizing antibodies can only be confirmed by a plate reduction neutralization test. However, it has been shown that the high titers of IgG antibodies detected by enzyme-linked immunosorbent assays (ELISA) are positively correlated with neutralizing antibodies. Also, specific IgA, IgM and IgG isotype antibodies to different viral proteins have been detected through ELISA [3]. IgM and IgG antibody assays based on ELISA have a higher specificity than 95% for diagnosing COVID-19. Thus, diagnosis by serology is becoming an important tool to understand the extent of COVID-19 in the healthcare community.

Healthcare workers (HCWs) are at high risk of infection owing to occupational exposure to patients and virus-contaminated surfaces [4]. Among them, dentists are at higher risk for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission because their work requires close physical contact with patients and dental procedures generate aerosols, which may pose potential risks to both operators and patients [5].

Several measures have been suggested for dental practitioners to contain the spread of COVID-19, such as use of personal protective equipment (PPE), procedures to reduce aerosol formation and use of high-velocity suction and rubber dental dams whenever possible [6].

Although there have been no reports of COVID-19 cases transmitted in dental settings, there is the possibility of infected dentists exposing patients and other healthcare workers, even if they are asymptomatic.

Some studies have suggested testing healthcare personnel every two weeks [7]. The choice of test frequency and type is influenced by the capacity and infrastructure available for performing tests, the variable incubation period of the infection (5 to 14 days) and the window of infectivity. Given the incorrect diagnostic impression in symptomatic, asymptomatic and paucisymptomatic individuals, the time involved in classic tests and the impossibility of implementing preventive isolation of all the healthcare personnel required during a pandemic, there is a need to validate rapid tests to speed up diagnosis and enable healthcare personnel to go back to work as quickly as possible. Rapid antigen and antibody detection tests, which are easy to perform, have recently been developed and recommended as a first-line diagnostic test.

Aim of the Study

The aim of the present study was to evaluate the validity of a commercial rapid serologic test for COVID-19 in a population of workers who provided services during the COVID-19 pandemic at a University Dental Hospital in the Buenos Aires Metropolitan area.

Materials and Methods

This study was conducted at the University Dental Hospital of the School of Dentistry of Buenos Aires University (FOUBA, according to its initials in Spanish) on a non-probabilistic sample of 284 FOUBA workers from clinical and nonclinical areas. The sample comprised persons of both sexes, over 21 years old, who provided essential services during the first 180 days of the COVID-19 pandemic (preventive mandatory social isolation period (PMSI) and voluntarily accepted to be tested.

After signing informed consent, each participant completed a medical history to enable collection of COVID-19 epidemiological data [8]. Two serologic tests were performed per subject to detect infection by SARS-CoV2: (1) Blood test for enzyme-linked immunosorbent assays (ELISA) using blood from peripheral venipuncture and processed with direct method (specificity 95% and sensitivity 85%) [9]; (2) Commercial rapid serologic test (Pambio™ COVID 19 IgG/IgM rapid test device. ABBOTT®) using capillary whole blood obtained by finger prick.

Rapid test preparation method: Finger was pricked with a sterile lancet, and 20 µL of the blood sample followed by 2 drops of buffer added to the device. After 10 - 20 minutes, the result was read, following the manufacturer's instructions.

The presence of anti-SARS-CoV-2 IgM and anti-SARS-CoV-2 IgG will be indicated by a red/pink test line in the M and G region. If

only the control line (C) shows red, the sample is negative. Either the M or the G line, or both, turning red indicates the presence of anti-SARS-CoV-2-IgM or anti-SARS-CoV-2-IgG or both antibodies in the specimen. If the control line does not appear red, the test is invalid and should be repeated with another cartridge.

Samples were collected, maintained and transported by trained, calibrated personnel and processed rapidly following the protocol at the Institute for Biomedical Research in Retrovirus and AIDS (Instituto de Investigaciones Biomédicas en Retrovirus y SIDA - IMBIRS/CONICET) of Buenos Aires University School of Medicine.

Subject age, sex and results of both tests were recorded. For this sample of clinical and nonclinical staff, the weighted prevalence of COVID-19 was 4% [16].

Ethical approval was not required for this study as only anonymous data were used and testing of healthcare workers was part of the dental school policies during the pandemic period.

Statistical analysis

The categorical data were described by absolute frequencies and percentages with 95% confidence intervals (CI95). The CI95 were estimated by the score method [10]. Age was described by mean, standard deviation (SD), median, first quartile (Q1), third quartile (Q3), minimum and maximum.

Frequencies were compared using the Chi-square test or Fisher's exact test with 5% significance level. The diagnostic accuracy of the Commercial rapid serologic test (Pambio™ COVID 19 IgG/IgM rapid test device. ABBOTT®) was evaluated using ELISA as the gold standard. The following measures were estimated: Sensitivity, Specificity, Positive predictive value, Negative predictive value, Positive likelihood ratio and Negative likelihood ratios [11]. The software used was Calc, from Apache OpenOffice™ v. 4.1.6 [12] and InfoStat v. 2020 [13] y R v. 4.0.3 [14] with epiR package [15].

Results

Demographics

The sample consisted of 284 subjects, including 183 female (64%; CI95: 59% to 68%) and 101 male (36%; CI95: 32% to 41%). Subject age ranged from 21 to 69 years, with mean (SD) 39 (11) and median (Q1-Q3) 36 (30 - 47). Distribution was not uniform (Chi-square = 75.15; df = 4; $p < 0.05$). The groups 20 to 29, 30 to 39 and 40 to 49 years were larger than the groups 50 to 59 and 60 or over. The largest age group in the sample was 30 to 39 years (35%; CI95: 30% to 41%) (Figure 1).

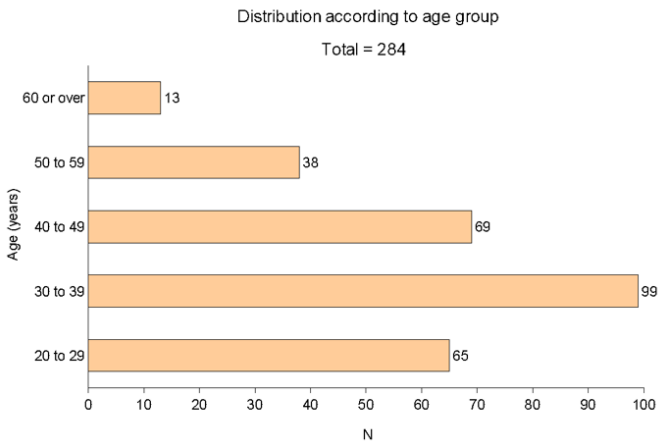

Figure 1: Distribution according to age group.

The diagnostic accuracy of the rapid test was determined by using ELISA as gold standard. We used the information of 284 subjects who were evaluated at the same time with both procedures.

Table 1 shows the absolute frequencies for the different combinations of tests used (rapid test/ELISA) and diagnoses obtained (positive/negative).

		ELISA		
		Positive	**Negative**	**Total**
Rapid test	Positive	4	30	34
	Negative	5	245	250
	Total	9	275	284

Table 1: *Results of the rapid tests and ELISA in 284 subjects evaluated with both.*

Table 2 shows the estimated measures. Rapid test sensitivity was 0.44 (CI95: 0.14 to 0.79), while its specificity was more than double (0.89; CI95: 0.85 to 0.93). Positive predictive value was 0.12 (CI95: 0.03 to 0.27), but negative predictive value was much higher

(0.98; CI95: 0.95 to 0.99). The positive and negative likelihood ratios were 4.07 (CI95: 1.82 to 9.11) and 0.62 (CI95: 0.35 to 1.12), respectively.

	Value	CI95
Sensitivity	44%	14 to 79%
Specificity	89%	85 to 93%
Positive predictive value	12%	3 to 27%
Negative predictive value	98%	95 to 99%
Positive likelihood ratio	4.07	1.82 to 9.11
Negative likelihood ratios	0.62	0.35 to 1.12

Table 2: *Measures of diagnostic accuracy of the rapid test, using ELISA as gold standard.*

Discussion

Epidemiologically, a key issue is finding asymptomatic and presymptomatic subjects in order to prevent community and nosocomial infection. Large dental clinics and schools of dentistry may be environments where testing would be critical because of the close contact between dental care workers and patients. There is a growing need for diagnostic tests for SARS-CoV-2 infection, which drives the development of different diagnostic resources such as antibody detection tests. However, there are few reports on evaluations of anti-SARS-CoV-2 antibody assays using appropriate reference assays for comparison [17].

The aim of this observational study was to evaluate the validity of a rapid test designed to detect anti-SARS-CoV-2 IgG and IgM antibodies from a capillary whole blood sample obtained by finger prick, in clinical and nonclinical staff from a dental teaching hospital. It found 89% for specificity and 44% for sensitivity, using enzyme linked immunosorbent assay (ELISA) as gold standard.

The sensitivity and specificity of rapid assays have recently been estimated in several studies performed with venous blood samples. Li., *et al*. [18] in the first report evaluating a rapid test for anti-SARS-CoV 2 antibodies that they developed at the beginning of the pandemic, reported sensitivity of 70.5% for IgG and 82.6% for IgM, and specificity of 98.4% for IgG and 91.4% for IgM. In contrast, our data are similar to those reported by Dohla., *et al*. [19] for evaluation of a rapid test (sensitivity 36.4% and specificity 88.9%).

With the aim of establishing variations according to time, Pan., *et al*. [20] observed sensitivity of 11.1% for IgG and 3.7% for IgM at 7 days, and sensitivity of 55.8% for IgG and 54.7% for IgM after 15 days. Prazuck., *et al*. [21] analyzed two rapid tests for antibodies, finding sensitivity values ranging from 10% to 35% during the first 10 days from the onset of the disease, reaching 100% after 15 days. In agreement with our study, published reports on performance of rapid tests report lower sensitivity for specific IgG and IgM than do the commercial specifications [17-23].

Currently, the response against SARS-CoV-2 is not well known. It is widely accepted that IgM is usually the first responder antibody. providing the first line of defense during viral infections, prior to the generation of adaptive, high-affinity IgG responses serving as the more robust long-term immunity. In all cases, the time in the evolution of the disease at which the test is performed modifies sensitivity, which is lower during the initial periods of infection. Several studies have evaluated sensitivity in hospitalized patients, and therefore it is not clear whether the tests can detect lower levels of antibodies such as those in mild or asymptomatic infections, which could be more frequent situations among active healthcare personnel.

In a previous report, our team estimated that the prevalence rate of SARS-CoV-2 infection among workers at the same institution was 4% during the initial isolation period established by national health authorities [16].

In that study, the diagnostic test's positive and negative predictive values were 12% and 98%, respectively. As prevalence of the disease was low (4%) in our sample, the positive predictive value would be low, and the negative predictive value would be high. However, positive and negative likelihood ratios were 4.07 and 0.62, respectively. These values are not high or low enough to establish diagnostic accuracy.

During the first week after the onset of symptoms, antibody assays have sensitivity that is too low to play a major role in diagnosing COVID-19, but they may still play a part as a complement to other assays in individuals tested later, when RT-PCR assays are negative [24]. Antibody assays are probably useful to detect a prior SARS-CoV-2 infection if they are used 15 or more days after the on-

set of symptoms. There is considerable room for improvement in the design, performance and presentation of reports on studies of the accuracy of rapid COVID-19 tests. Studies should report data on sensitivity broken down according to time from the onset of symptoms [23].

This study has several limitations. We could not evaluate variations in the humoral response because we were unable to test subjects more than once. Another limitation is related to variations in antibody response according to age and certain conditions such as immunodeficiency disorders. Lastly, our sample comprised subjects with low prevalence of the infection, as they were performing regular tasks. This affects the positive and negative predictive value of the test.

Despite these limitations, this rapid serologic test was very specific (no false positive) and had high negative predictive value. As this kind of test is easy to use, it could prove useful within healthcare facilities to determine seroprevalence in a large asymptomatic population. The test is simple, qualitative, and provides a result within 15 minutes.

Conclusion

This rapid serologic test was very specific and had low sensitivity. Although it could be used for monitoring previous exposure to COVID-19 in dental care workers, it should only be used in environments with inadequate access to more complex diagnostic tools. This method should not be used as the sole basis for treatment or other management decisions. The development of new rapid tests will be particularly interesting for low-resource settings or any other sites where lab tests are a less obvious choice.

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Volume 4 Issue 6 June 2021