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## RESEARCH ARTICLE

### Are rapid antigen detection tests capable of detect different SARS-COV-2 variants?

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#### Abstract

Rapid Antigen Detection Tests can be a good approach to in time SARS-CoV-2 detection as they are easy to use and provide a result in few minutes. However, they have shown to have lower sensitivities than desirable for a diagnostic technique that has come to be used for mass screening. With the aim of continuing to define the limits of RAgDT, their possible variability of sensitivity has been analysed against different variants of SARS-CoV-2.

In this study, three different Tests from different manufacturers (Abbott, Roche and Lambra) were tested with a set of 100 nasopharyngeal samples, of which 93 were determined as positive by RT-qPCR and 7 as negative.

Total sensitivities were: 72.04% for Abbott and 59.14% both for Roche and Lambra. Attending to variants, the three with higher sensitivity were: Alfa, Omicron and Delta (Abbott); Alfa, Omicron and Mu (Roche) and Alfa, Beta and Gamma (Lambra). Results show great variability between the tests analysed, which reinforces the idea that any negative diagnosis made with them should be taken with caution, especially in seasons of alternating circulation of variants.

**Keywords:** SARS-CoV-2; Rapid antigen detection test; Variant sensibility; Variant detection

## Introduction

From the very beginning of SARS-Cov-2 pandemic<sup>1</sup>, it has stressed our public health system, even when the isolation, sequencing, identification as a SARS-like Coronavirus member and genetic characterization were achieved in few days<sup>2</sup>, something that has conducted to development of rapid and easy tests in order to diagnose all possible infected patients.

Nowadays and after the spread of different variants of the SARS-CoV-2 (first variant of care was detected around September of 2020<sup>3</sup>), all the attention is putting on the possibility they can be more infective or that vaccines can be affected<sup>4,5</sup>, but what about the diagnostics techniques based on antigen detection?

Even when some studies have been indicating that sensitivity of Rapid Antigen Detection Test (RAgDT) is not as high as it would be desirable<sup>6,7</sup>, they have been a useful instrument for patients triage on some situations, even currently being marketed for self-diagnosis at home<sup>8,9</sup>.

However, being a diagnostic technique based on the detection of viral proteins and considering the fact that these have been changing as the virus has evolved during the pandemic<sup>10</sup>, it is worth asking how these changes could have affected sensitivity of the RAgDT, taking into account that in other aspects influenced by these changes, such as vaccines, there have been various setbacks<sup>11</sup>.

So the aim of this study is to know if three different RAgDT are able to detect different

SARS-CoV-2 VOC and VOI circulating among the population.

## Material and Methods

**Samples:** between June 2021 and January 2022, 100 different clinical nasopharyngeal samples were collected from different adult patients with SARS-CoV-2 infection suspicion. Of this set of samples, 93 were identified as SARS-CoV-2 positive; average cycle threshold (Ct) value of these samples was  $27.04 \pm 4.73$  (range 16 – 35; CI 95% 26.08 – 28.00) and average viral load was  $6.25 \pm 1.81$  (range 2.66 - 12.27; CI 95% 5.88 - 6.62).

Among these positives the following variants were detected: 16 Alpha (lineage 2.1.1.7), 14 Beta (lineage B.1.351), 12 Gamma (lineage P.1), 18 Delta (lineage B.1.617.2), 7 Lambda (lineage C.37), 8 Mu (lineage B.1.621) and 18 Omicron (lineage B.1.1.529).

**SARS-CoV-2 detection:** all samples were processed by the protocols of the laboratory for SARS-CoV-2 detection and variant identification<sup>12,13</sup>. Genome extraction was performed in a MagNaPure 96 automatic robot (Roche; Geneva, Switzerland) and genome detection was performed with a multiple qRT-PCR directed to two regions of the SARS-CoV 2 genome (Orf1ab and N gene), as well as the human  $\beta$  globin gen. Variant detection was performed by allelic discrimination.

**Rapid Antigen Detection Tests:** for this study, three rapid antigen detection tests available on the market were tested: Panbio Covid-19 Ag rapid test device (Abbott,

Germany), SARSCoV2 Rapid Antigen test (Roche, Germany) and Test Rápido COVID-19 Ag (Lambra, Spain). All tests were performed following the manufacturer's instructions.

**Statistical analysis:** an ANOVA test was performed between the means of the positive samples detected by the three RAgDTs, both by Ct and by viral load, to verify the existence of significant differences between the tests in the detection of all the samples as well as for each variant.

#### Results:

Of the 100 samples that were tested by IC (93 positive and 7 negative) to analyse sensitivity based on SARS-CoV-2 variant, Abbott detected 67 (72.04%) and both Roche and Lambra detected 55 (59,14%).

Attending to variants, Abbott showed sensitivities between 57.10% for the Lambda variant (n=4) and 87.50% for Alpha (n=14); Roche was between 42.86% for Lambda (n=3) and 68.75% for Alpha (n=11); and Lambra between 37.50% for Mu (n=3) and 75% for Alpha (n=12).

On the other hand, taking care of Ct results, it can be found that total average of the detected samples on each RAgDT are 2 – 3 cycles lower than total samples average, being  $25.27 \pm 5.10$  (Abbott),  $24.27 \pm 3.87$  (Roche) and  $24.46 \pm 3.87$  (Lambra). Similar results were found for viral load average (about 1 log higher), with only Lambra managing to detect samples with logarithms less than 4.

The seven PCR-negative samples were also negative for the three antigenic tests used, with a specificity of 100%.

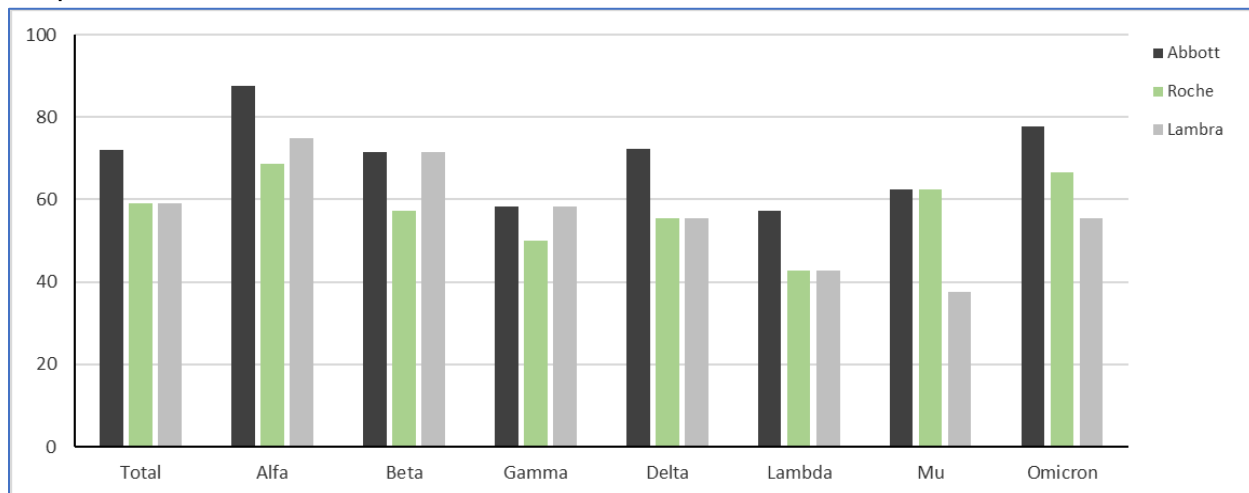
After the comparative statistical analysis of the means of the total and of each variant analysed by each RAgDT, no significant differences were found.

All these results, expressed by Cycle Threshold (Ct), are shown in Table 1 and Graphics 1 and 2.

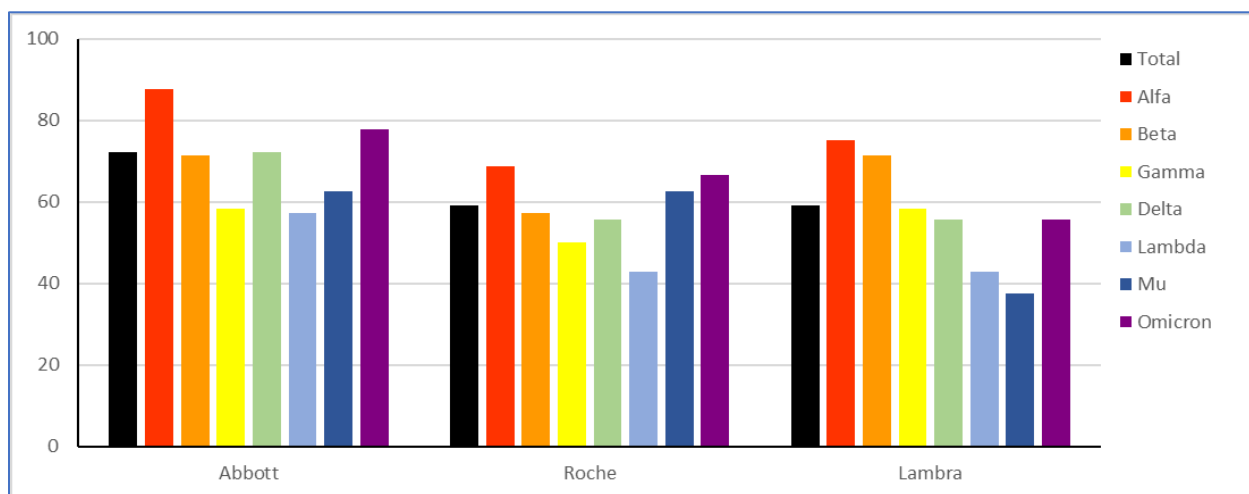
Table 1: Sensitivity, average, range and CI 95% for each SARS-CoV-2 variant for the three RAgDT analysed, distributed by cycle threshold and viral load.

RAgDT	Variant	Samples	Sensitivity	Cycle threshold (Ct)				Viral Load (log)			
				$\bar{X} \pm \sigma$	Range	CI 95%	p-value	$\bar{X} \pm \sigma$	Range	CI 95%	p-value
Abbott	Total	93	67 (72.04%)	25.27 ± 5.10	(16 - 33)	(24.05 - 26.49)	0.40	6.90 ± 1.58	(4.15 - 12.27)	(6.52 - 7.28)	0.50
	Alfa	16	14 (87.50%)	24.50 ± 3.59	(18 - 30)	(22.74 - 26.26)	0.71	7.13 ± 1.08	(5.51 - 9.26)	(6.56 - 7.70)	0.47
	Beta	14	10 (71.43%)	24.90 ± 5.24	(19 - 32)	(22.16 - 27.64)	0.79	7.17 ± 1.73	(4.55 - 8.96)	(6.10 - 8.24)	0.73
	Gamma	12	7 (58.33%)	25.20 ± 2.39	(20 - 28)	(23.85 - 26.55)	0.79	5.17 ± 0.78	(4.15 - 6.80)	(4.59 - 5.75)	0.79
	Delta	18	13 (72.22%)	24.27 ± 4.96	(16 - 33)	(21.98 - 26.56)	0.76	7.49 ± 2.15	(4.73 - 12.27)	(6.32 - 8.66)	0.82
	Lambda	7	4 (57.14%)	25.75 ± 6.45	(18 - 32)	(20.97 - 30.53)	0.88	6.36 ± 2.13	(4.32 - 9.23)	(4.27 - 8.45)	0.88
	Mu	8	5 (62.50%)	26.00 ± 2.65	(23 - 29)	(24.17 - 27.83)	0.65	6.62 ± 0.79	(5.73 - 7.76)	(5.93 - 7.31)	0.64
	Omicron	18	14 (77.78%)	27.08 ± 3.32	(23 - 33)	(25.55 - 28.61)	0.39	6.51 ± 0.97	(4.76 - 7.76)	(6.00 - 7.02)	0.39
Roche	Total	93	55 (59.14%)	24.27 ± 3.87	(16 - 32)	(23.25 - 25.29)	0.40	7.23 ± 1.53	(4.15 - 12.27)	(6.83 - 7.63)	0.50
	Alfa	16	11 (68.75%)	23.36 ± 3.11	(18 - 30)	(21.84 - 24.88)	0.71	7.64 ± 0.94	(5.66 - 9.26)	(7.09 - 8.19)	0.47
	Beta	14	8 (57.14%)	23.50 ± 4.90	(19 - 32)	(20.93 - 26.07)	0.79	7.69 ± 1.49	(5.18 - 8.96)	(6.63 - 8.69)	0.73
	Gamma	12	6 (50.00%)	24.75 ± 2.50	(20 - 28)	(23.34 - 26.16)	0.79	5.27 ± 0.86	(4.15 - 6.80)	(4.58 - 5.96)	0.79
	Delta	18	10 (55.55%)	23.00 ± 4.72	(16 - 29)	(20.82 - 25.18)	0.76	7.97 ± 2.17	(5.69 - 12.27)	(6.62 - 9.32)	0.82
	Lambda	7	3 (42.86%)	23.67 ± 6.03	(18 - 30)	(19.20 - 28.14)	0.88	7.04 ± 2.01	(5.29 - 9.23)	(4.77 - 9.31)	0.88
	Mu	8	5 (62.50%)	26.00 ± 2.65	(23 - 29)	(24.17 - 27.83)	0.65	6.62 ± 0.79	(5.73 - 7.76)	(5.93 - 7.31)	0.64
	Omicron	18	12 (66.67%)	26.40 ± 2.99	(23 - 31)	(25.02 - 27.78)	0.39	6.71 ± 0.87	(5.36 - 7.76)	(6.22 - 7.20)	0.39
Lambra	Total	93	55 (59.14%)	24.46 ± 3.87	(16 - 32)	(23.37 - 25.49)	0.40	7.13 ± 1.65	(3.55 - 12.27)	(6.70 - 7.56)	0.50
	Alfa	16	12 (75.00%)	23.91 ± 3.53	(18 - 30)	(22.18 - 25.64)	0.71	7.46 ± 1.08	(5.51 - 9.26)	(6.85 - 8.07)	0.47
	Beta	14	10 (71.43%)	25.10 ± 5.49	(19 - 32)	(22.23 - 27.97)	0.79	7.09 ± 1.83	(4.55 - 8.96)	(5.96 - 8.22)	0.73
	Gamma	12	7 (58.33%)	25.80 ± 3.19	(20 - 30)	(23.99 - 27.61)	0.79	4.93 ± 1.07	(3.55 - 6.80)	(4.13 - 5.73)	0.79
	Delta	18	10 (55.55%)	23.00 ± 4.72	(16 - 29)	(20.82 - 25.18)	0.76	7.97 ± 2.17	(5.69 - 12.27)	(6.62 - 9.32)	0.82
	Lambda	7	3 (42.86%)	23.67 ± 6.03	(18 - 30)	(19.20 - 28.14)	0.88	7.04 ± 2.01	(5.29 - 9.23)	(4.77 - 9.31)	0.88
	Mu	8	3 (37.50%)	24.50 ± 0.71	(23 - 25)	(24.01 - 24.99)	0.65	7.07 ± 0.21	(6.92 - 7.76)	(6.83 - 7.31)	0.64
	Omicron	18	10 (55.56%)	25.37 ± 2.33	(23 - 29)	(24.30 - 26.44)	0.39	7.01 ± 0.68	(5.96 - 7.76)	(6.59 - 7.43)	0.39

Graphic 1: Sensitivities obtained for each RAgDT distributed by SARS-CoV-2 variant.



Graphic 2: Sensitivities obtained for each SARS-CoV-2 variant distributed by RAgDT.



**Discussion:**

As one of the most used techniques for SARS-CoV-2 detection, knowing the limits of the different rapid antigen detection tests can improve management of themselves for patient triage, especially now, when there are more and more variants of care around the world.

As we can see, total sensitivity for SARS-CoV-2 samples is not different than founded in other similar studies, as the ones carried by

Alber<sup>6</sup>, Fenollar<sup>14</sup>, Krüttgen<sup>15</sup> and Corman<sup>16</sup>, or even ourselves<sup>7</sup>, either based on cycle threshold or viral load, with this one showing no detection on the low values (lower than 4 log). And, as these studies shown, real sensitivity of these kind of tests are far away from the gold-standard, the RT-qPCR.

Also, the fact that higher Ct or lower viral loads can not be detected easy by RAgDT, in this new study, reinforces the idea<sup>7</sup> that these tests should not be used for massive

screening, given the possibility of missing false negatives in those Ct or viral loads ranges, that were at the beginning of the infection instead of at the end, developing infectious in few days.

However, with the results expressed before, it is true that all tests checked can detect a range of seven different variants of SARS-CoV-2, including the most widely distributed around the world nowadays (Omicron), and six deescalated variants, including 4 old VOC (Alfa, Beta, Gamma and Delta) and two old VOI (Lambda and Mu)<sup>17</sup>.

Attending to variants results, the three tests performed share that the highest sensitivity shown is for Alfa variant (87.5% Abbott; 68.75% Roche and 75% Lambra), the first VOC detected in the world, while the other four principal variants are slightly lower.

A possible explanation for this could be the fact that the development, fine-tuning, and distribution to patient care points of the first RAgDT coincided in time with the spread of the Alpha variant of SARS-CoV-2<sup>18,19</sup>; therefore, the fact that the lower sensitivity detected for the rest of the analysed variants, which subsequently emerged supplanting each other until reaching the current Omicron BA3, BA4 and BA5<sup>17</sup>, highlights the need to maintain a review of the RAgDTs, as well as it was done for vaccines<sup>11</sup>, as they are also based on the recognition of viral proteins.

Moreover, this can be more important now than before, since at first, RAgDTs were only performed at patient care points by health personnel, but now these can be purchased in

person at pharmacies and other points of sale for self-diagnosis<sup>8,9</sup>.

Knowing that the general sensitivity of these tests is lower than the announced, especially when it comes to detecting low viral loads, which can occur at the beginning of the infection, with which a false negative would give a false sense of security to the self-diagnosed patient, the fact that the sensitivity also varies depending on the variant of the virus opens the door to a possible greater indeterminacy in the face of new variants.

For this reason, it is very important that the information available on this type of test be presented to the population in a clear and concise manner, so that people can act accordingly to the available knowledge, a task that is the responsibility of scientists and healthcare professionals in the same way.

#### Conclusions:

1. Even when global sensitivity of rapid antigen detection tests is far from the desirable, they can recognize a wide range of SARS-CoV-2 variants.
2. The difference in sensitivity between variants raises doubts for the future if antigen detectors do not keep updating with the new variants.
3. The fact that RAgDT diagnosis has been decentralized implies the need to make the population aware of the limitations of these tests.

## DECLARATIONS

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- **Authors' contributions:**  
All authors have contributed equally to this paper.
- **Consent for publication:**  
All authors have expressed their consent for the publication of this paper.

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