Received: 8 April 2021 | Revised: 11 May 2021 | Accepted: 13 May 2021

DOI: 10.1002/jmv.27089

SHORT COMMUNICATION

JOURNAL OF MEDICAL VIROLOGY WILEY

Comparative evaluation of Panbio and SD Biosensor antigen rapid diagnostic tests for COVID-19 diagnosis

Felipe Pérez-García[1] | Juan Romanyk[1,2] | Helena Moya Gutiérrez[1] | Andrea Labrador Ballestero[1] | Inés Pérez Ranz[1] | Javier González Arroyo[1] | Victoria González Ventosa[1] | Ramón Pérez-Tanoira[1,2] | Concepción Domingo Cruz[1] | Juan Cuadros-González[1,2]

[1]Servicio de Microbiología Clínica, Hospital Universitario Príncipe de Asturias, Madrid, Spain

[2]Departamento de Biomedicina y Biotecnología, Facultad de Medicina, Universidad de Alcalá de Henares, Alcalá de Henares, Spain

Correspondence
Felipe Pérez-García, Hospital Universitario Príncipe de Asturias, Servicio de Microbiología Clínica. Carretera de Alcalá, s/n, 28805 Meco, Madrid, Spain.
Email: felipe.perez.garcia.87@gmail.com

Abstract

The aim of our study was to evaluate the diagnostic performance of two antigen rapid diagnostic tests (Ag-RDTs) to diagnose severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. We evaluated *Panbio* and *SD-Biosensor* Ag-RDTs. We employed 186 polymerase chain reaction (PCR) negative samples to evaluate the specificity and 170 PCR positive samples to assess the sensitivity. We evaluated their sensitivity according to Cycle threshold (C_t) values and days post onset of symptoms (d.p.o.). Tests were compared using the McNemar's test. Agreement was evaluated using the *kappa* score. Specificity was 100% for *Panbio* and 97.3% for *SD-Biosensor*. Sensitivity for samples with $C_t \leq 20$ was 100% for both assays and for samples with $C_t = 20–25$ was 93.0% (*Panbio*) and 95.3% (*SD-Biosensor*) ($p = 1.000$). Sensitivity decreased for samples wit $C_t = 25–30$ (*Panbio*: 41.3%, *SD-Biosensor*: 52.2%, $p = 0.125$) and samples with $C_t \geq 30$ (*Panbio*: 5.0%, *SD-Biosensor*: 17.5%, $p = 0.063$). Sensitivity within seven d.p.o. was 87.7% for Panbio and 90.4% for SD-Biosensor and notably decreased after seven d.p.o. Agreement with PCR was excellent for high viral load samples ($C_t \leq 25$): *Panbio*, 98.9%, *kappa* = 0.974; *SD-Biosensor*, 97.4%, *kappa* = 0.940. Agreement between Ag-RDTs was excellent (94.9%, *kappa* = 0.882). *Panbio* and *SD-Biosensor* Ag-RDTs showed excellent agreement and diagnostic performance results for samples with high viral loads ($C_t \leq 25$) or samples within seven d.p.o.

KEYWORDS

antigen rapid diagnostic test, COVID-19, lateral flow immunoassay, Panbio COVID-19 Ag, SARS-CoV-2, SD biosensor COVID-19 Ag FIA

1 | INTRODUCTION

The pandemic due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become one of the main global economic and health priorities. Viral RNA detection in respiratory samples using polymerase chain reaction (PCR) is the current reference method for coronavirus disease 2019 (COVID-19) diagnosis. However, they are not useful as point of care (POC) tests due to an excessive turnaround time for results.[1,2] Antigen rapid diagnostic tests (Ag-RDTs) have been developed as alternative tests to PCR for COVID-19 symptomatic patients, as they could be employed as POC tests, presented a lower cost than PCR assays and could improve the turnaround time for results. Moreover, some authors have shown that these advantages could overcome the sensitivity limitation, especially where PCR is unavailable or where prolonged turnaround times preclude clinical utility.[3-5] Our objective was to evaluate the diagnostic performance of two of these commercialized Ag-RTDs.

2 | METHODS

2.1 | Population and study period

The study was performed between 1 and 30 December 2020. We included 356 nasopharyngeal samples, which were submitted in 3 ml of universal transport medium (UTM). Each sample corresponded to one single patient and we included 186 PCR negative samples and another 170 PCR positive samples.

2.2 | Diagnostic techniques

RNA amplification was performed using three Real-Time PCR platforms: *Allplex SARS-CoV-2 assay* (Seegene, which detected SARS-CoV-2 *E*, *N* and *RdRP* genes), *Viasure SARS-CoV-2 Real Time PCR Detection Kit* (Certest Biotech S.L.; detected genes: *ORF1ab* and *N*) and *GeneFinder COVID-19 Plus RealAmp Kit* (Osang Healthcare Co.; detected genes: *E*, *N* and *RdRP*). Nasopharyngeal samples were tested using one or another PCR platform indistinctly, according to the usual laboratory workflow. Samples were considered as positive when amplification was detected for all genes included inf each RT-PCR assay. Reliability of these three platforms had been previously evaluated in our laboratory, showing 100% agreement and quite similar C_t values in the results for those samples that amplified all the targets covered by each technique (see Table S1).

Regarding Ag-RDTs, we evaluated two Ag-RDTs that detected SARS-CoV-2 nucleoprotein antigens: *Panbio COVID-19 Ag Rapid Test Device* (Abbot Rapid Diagnostics GmbH, Jena) and *SD-Biosensor STANDARD F COVID-19 Ag FIA* (SD Biosensor, Inc.). Lecture of the results was optical for *Panbio* and by immunofluorescence using a *STANDARD F2400* analyzer (SD Biosensor, Inc.) for *SD-Biosensor* Ag-RDT.

All equipments were used according to the manufacturer's instructions for both the handling and the interpretation of the results.

2.3 | Clinical data

Clinical variables of the study population (time from the onset of symptoms) were obtained from the medical records. We assessed SARS-CoV-2 viral load using the *Cycle threshold* (C_t) value corresponding to N gene for all PCR positive samples.[6]

2.4 | Statistical analysis

Categorical variables were expressed as proportions and continuous variables as median and interquartile range (IQR) and. Sensitivity and specificity with 95% confidence intervals (95% CI) were calculated using RT-PCR as gold standard. Sensitivity was evaluated globally and also according to the C_t value for N gene[7] using different cutoffs (high viral load samples: $C_t \leq 20$ and $C_t = 20–25$; low viral load samples: $C_t = 25–30$ and $C_t > 30$) and the days post onset of sypmtoms (d.p.o.), using a cutoff of 7 days (≤ 7 days, 7–14 days, >14 days). Agreement between techniques was evaluated using the Cohen's *kappa* score[8] and the McNemar's test. For these comparisons, a *p* value less than or equal to 0.05 was considered significant. Statistical analysis was performed using Stata/IC 13.1 (StataCorp).

3 | RESULTS

Diagnostic performance results according C_t values are summarized in Table 1 and Figure S1. Specificity was 100% for *Panbio* and 97.3% for *SD-Biosensor*, due to five PCR negative samples that were positive for this assay. Overall sensitivity was 60.0% for *Panbio* and 66.5% for *SD-Biosensor* and this difference was statistically significant ($p = 0.003$). Sensitivity was higher for samples with high viral loads, reaching 100.0% for samples with $C_t \leq 20$ for both tests. For samples with $C_t = 20–25$, sensitivity was 93.0% for *Panbio* and 95.3% for *SD-Biosensor* ($p = 1.000$). Sensitivity significantly decreased for low viral load samples: for C_t values between 25 and 30, sensitivity was 41.3% for *Panbio* and 52.2% for *SD-Biosensor* ($p = 0.125$), and for C_t values over 30, sensitivity was 5.0% for *Panbio* and 17.5% for *SD-Biosensor* ($p = 0.063$). There were no significant differences on sensitivity results between Ag-RDTs according C_t values (Table 1).

Regarding symptoms of those 170 PCR positive patients, information regarding symptoms was unavailable for 10 patients. For the remaining 160 cases, 134 (83.7%) patients presented COVID-19 symptoms and 26 (16.3%) were asymptomatic. Information about time from the onset of symptoms to sample obtention was unavailable for another six symptomatic patients. Table 2 and Figure S2 summarize the diagnostic performance results according to the time from the onset of symptoms. Both Ag-RDTs showed high values of sensitivity in samples taken within the first seven d.p.o. (87.7% for *Panbio*, and 90.4% for *SD-Biosensor*, $p = 0.625$). Sensitivity decreased significantly from the eighth d.p.o., reaching a sensitivity of 31.0% for *Panbio* and 38.1% for *SD-Biosensor* for day 8%–14% and 30.8% for *Panbio* and 38.5% for *SD-Biosensor* from 14 days. There were no significant differences on sensitivity results between Ag-RDTs according d.p.o. (Table 2).

Finally, regarding agreement results, agreement of Ag-RDTs with PCR was moderate in overall samples (agreement = 80.9%, $k = 0.596$ for *Panbio*; 82.6%, $k = 0.646$ for *SD-Biosensor*) but it was excellent for high viral load samples ($C_t \leq 25$) for both Ag-RDTs (*Panbio*: 98.9%, $k = 0.974$, *SD-Biosensor*: 97.4%, $k = 0.940$). Moreover, agreement between Ag-RDTs was excellent for overall samples (94.9%, $k = 0.882$)

TABLE 1 Diagnostic performance of the evaluated Ag-RDTs according to viral load

Type of sample	C_t values	Panbio		SD-Biosensor		*p* value
PCR negative	N/A	Positive samples	0/186	Positive samples	5/186	0.063
(*n* = 186)		Specificity	100.0	Specificity	97.3	
			(98.0 – 100.0)		(93.8–99.1)	
PCR positive	25.2 (20.2– 29.7)	Positive samples	102/170	Positive samples	113/170	**0.003**
		Sensitivity	60.0	Sensitivity	66.5	
(*n* = 170)			(52.2 – 67.4)		(58.8–73.5)	
High viral load samples						
C_t≤20	17.8 (16.8– 18.5)	Positive samples	41/41	Positive samples	41/41	1.000
		Sensitivity	100.0	Sensitivity	100.0	
(*n* = 41)			(91.4 – 100.0)		(91.4–100.0)	
C_t = 20–25	22.1 (20.8– 23.6)	Positive samples	40/43	Positive samples	41/43	1.000
		Sensitivity	93.0	Sensitivity	95.3	
(*n* = 43)	(80.9 – 98.5)		(84.2–99.4)			
Low viral load samples						
C_t = 25–30	27.2 (26.0– 28.7)	Positive samples	19/46	Positive samples	24/46	0.125
		Sensitivity	41.3	Sensitivity	52.2	
(*n* = 46)			(27.0 – 56.8)		(36.9–67.1)	
C_t > 30	31.3 (30.6 – 33.3)	Positive samples	2/40	Positive samples	7/40	0.063
(*n* = 40)		Sensitivity	5.0	Sensitivity	17.5	
			(0.6 – 16.9)		(7.3–32.8)	

Note: Statistics: values are expressed as absolute count (percentage) and median (interquartile range). Sensitivity and specificity results are expressed as percentage with 95% CI. P-values were calculated by the McNemar's test. Significant differences are shown in bold.

Abbreviations: Ag-RDT, antigen rapid diagnostic test; C_t, cycle threshold; N/A, not applicable; 95% CI, 95% confidence interval; p-value, level of significance.

TABLE 2 Diagnostic performance of the evaluated Ag-RDTs according to time form the onset of symptoms

Time from the onset of symptoms	Days	Panbio		SD-Biosensor		*p* value
≤7 days	4 (2 – 6)	Positive samples	64/73	Positive samples	66/73	0.625
(*n* = 73)		Sensitivity	87.7	Sensitivity	90.4	
			(77.9– 94.2)		(81.2 – 96.1)	
8–14 days	9 (8 – 11)	Positive samples	13/42	Positive samples	16/42	0.250
		Sensitivity	31.0	Sensitivity	38.1	
(*n* = 42)			(17.6– 47.1)		(23.6 – 54.4)	
>14 days	16 (15 – 18)	Positive samples	4/13	Positive samples	5/13	1.000
(*n* = 13)		Sensitivity	30.8	Sensitivity	38.5	
			(9.1 – 61.4)		(13.9 – 68.4)	

Note: Statistics: sensitivity results are expressed as percentage with 95% CI. P-values were calculated by the McNemar's test. No *p*-value was statistically significant ($p < 0.05$).

Abbreviations: Ag-RDT, antigen rapid diagnostic test; 95% CI, 95% confidence interval; *p*-value, level of significance.

being even better when we focused in high viral load samples (97.8%, $k = 0.948$).

4 | DISCUSSION

Ag-RDTs have demonstrated their reliability as diagnostic tools to aid in the control of SARS-CoV-2 pandemic. Although *Panbio* Ag-RDT has been the most frequently evaluated test,[7,9-12] the number of commercialized assays is growing exponentially.[10,13-17] Our results show that *Panbio* and *SD-Biosensor* Ag-RDTs are reliable to diagnose SARS-CoV-2 infection, as they fulfilled the general recommendations for the use of these tests that are recommended by the WHO ≥ 80% sensitivity and ≥97% specificity compared with PCR.[5,18] Moreover, they showed excellent performance within the first seven d.p.o. or when they are performed in samples with high viral load as well as excellent levels of agreement between them. Diagnostic performance of Ag-RDTs within the first 7 d.p.o. could be attributed to higher viral loads that are observed in these samples, as compared with samples obtained several days later, which is evidenced by observing the increasing trend of the median Cts values according to d.p.o. (see Figure S3).

Some authors have shown that, besides the lower sensitivity of Ag-RDTs compared with PCR, they improve the turnaround time for results, which is key to interrupt transmission chains to control the spread of this pandemic.[3,4,18,19] As a consequence, several diagnostic algorithms already recommend the use of these tests as first step for symptomatic patients within the first 57 days after the onset of symptoms[18-20] and our results support the use of *Panbio* and *SD-Biosensor* tests for that purpose. Some authors have pointed out that Ag-RDTs could also be reliable for detecting asymptomatic patients with high infectious capacity.[9] These findings would support the use of Ag-RDTs as screening test for massive population testing. However, more studies are needed to ensure the effectiveness of these tools for that purpose.

Our study presents some limitations: it is a retrospective study that has been conducted in a single institution and we have analyzed the results of two among all commercialized Ag-RDTs. Consequently, our conclusions should not be extrapolated to other available Ag-RDTs and more prospective multicenter studies and meta-analysis are needed to establish the usefulness of other Ag-RDTs. However, to the best of our knowledge, our work constitutes the first comparative evaluation of *Panbio* and *SD-Biosensor* Ag-RDTs and our findings indicate that these assays could be reliable tools for the early diagnosis of symptomatic COVID-19 cases and the control of this pandemic.

ACKNOWLEDGEMENTS

The authors thank Rebeca Bailén for her help with the preparation of the manuscript.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

ETHICS STATEMENT

The study was conducted according to the ethical requirements established by the Declaration of Helsinki. The Ethics Committee of Hospital Universitario Príncipe de Asturias (Madrid) approved the study (Protocol nº: Antigeno-COVID). Since the present study is retrospective, informed consent was not required.

AUTHOR CONTRIBUTIONS

Study concept and design: Felipe Pérez-García and Juan Cuadros-González. *Clinical data acquisition and interpretation of data*: Juan Romanyk, Inés Pérez Ranz, Andrea Labrador Ballestero, Helena Moya Gutiérrez, Javier Conzález Arroyo, Victoria González Ventosa and Concepción Domingo Cruz. *Statistical analysis*: Felipe Pérez-García. *Drafting of the manuscript*: Felipe Pérez-García and Juan Cuadros-González. *Supervision, critical revision of the manuscript for relevant intellectual content*: Juan Cuadros-González. All authors read and approved the final manuscript.

ORCID

Felipe Pérez-García http://orcid.org/0000-0002-4885-4334
Ramón Pérez-Tanoira http://orcid.org/0000-0002-9816-3208

REFERENCES

1. Vashist SK. In vitro diagnostic assays for COVID-19: recent advances and emerging trends. *Diagnostics*. 2020;10(4):202. https://doi.org/10.3390/diagnostics10040202
2. Vandenberg O, Martiny D, Rochas O, van Belkum A, Kozlakidis Z. Considerations for diagnostic COVID-19 tests. *Nat Rev Microbiol*. 2020;19:171-183. https://doi.org/10.1038/s41579-020-00461-z
3. Mina MJ, Parker R, Larremore DB. Rethinking Covid-19 test sensitivity—a strategy for containment. *N Engl J Med*. 2020;383:e120. https://doi.org/10.1056/NEJMp2025631
4. Larremore DB, Wilder B, Lester E, et al. Test sensitivity is secondary to frequency and turnaround time for COVID-19 surveillance. *medRxiv*. 2020. Published online ahead of print. https://doi.org/10.1101/2020.06.22.20136309
5. World Health Organization. Antigen-detection in the diagnosis of SARS-CoV-2 infection using rapid immunoassays; 2021. https://www.who.int/publications/i/item/antigen-detection-in-the-diagnosis-of-sars-cov-2infection-using-rapid-immunoassays. Accessed October 1, 2021
6. Lee S, Kim T, Lee E, et al. Clinical course and molecular viral shedding among asymptomatic and symptomatic patients with SARS-CoV-2 infection in a community treatment center in the Republic of Korea. *JAMA Intern Med*. 2020;180(11):1447-1452. https://doi.org/10.1001/jamainternmed.2020.3862.
7. Linares M, Pérez-Tanoira R, Carrero A, et al. Panbio antigen rapid test is reliable to diagnose SARS-CoV-2 infection in the first 7 days after the onset of symptoms. *J Clin Virol*. 2020;133:104659. https://doi.org/10.1016/j.jcv.2020.104659
8. McHugh ML. Interrater reliability: the kappa statistic. *Biochem Med (Zagreb)*. 2012;22(3):276-282.
9. Alemany A, Baró B, Ouchi D, et al. Analytical and clinical performance of the panbio COVID-19 antigen-detecting rapid diagnostic test. *J Infect*. 2021:S0163445321000049. 82(5):186–230. https://doi.org/10.1016/j.jinf.2020.12.033
10. Dinnes J, Deeks JJ, Adriano A, et al. Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection. Cochrane Infectious Diseases Group, ed. *Cochrane Database Syst Rev*. 2020;8 https://doi.org/10.1002/14651858.CD013705

11. Fenollar F, Bouam A, Ballouche M, et al. Evaluation of the Panbio Covid-19 rapid antigen detection test device for the screening of patients with Covid-19. *J Clin Microbiol*. 2020;59(2):e02589-20. https://doi.org/10.1128/JCM.02589-20
12. Pérez-García F, Romanyk J, Gómez-Herruz P, et al. Diagnostic performance of CerTest and Panbio antigen rapid diagnostic tests to diagnose SARS-CoV-2 infection. *J Clin Virol*. 2021;137:104781. https://doi.org/10.1016/j.jcv.2021.104781
13. Cerutti F, Burdino E, Milia MG, et al. Urgent need of rapid tests for SARS CoV-2 antigen detection: evaluation of the SD-Biosensor antigen test for SARS-CoV-2. *J Clin Virol*. 2020;132:104654. https://doi.org/10.1016/j.jcv.2020.104654
14. Mak GC, Cheng PK, Lau SS, et al. Evaluation of rapid antigen test for detection of SARS-CoV-2 virus. *J Clin Virol*. 2020;129:104500. https://doi.org/10.1016/j.jcv.2020.104500
15. Lambert-Niclot S, Cuffel A, Le Pape S, et al. Evaluation of a rapid diagnostic assay for detection of SARS-CoV-2 antigen in nasopharyngeal swabs. *J Clin Microbiol*. 2020;58(8):e00977-20. https://doi.org/10.1128/JCM.00977-20
16. Iglói Z, Velzing J, van Beek J, et al. Clinical Evaluation of Roche SD Biosensor Rapid Antigen Test for SARS-CoV-2 in Municipal Health Service Testing Site, the Netherlands. *Emerging Infectious Diseases*. 2021; 27 (5):1323–1329. http://dx.doi.org/10.3201/eid2705.204688
17. Mertens P, De Vos N, Martiny D, et al. Development and potential usefulness of the COVID-19 Ag Respi-Strip diagnostic assay in a pandemic context. *Front Med*. 2020;7:225. https://doi.org/10.3389/fmed.2020.00225. Accessed November 21, 2020.
18. EUROPEAN COMISSION. COMMISSION RECOMMENDATION of 18.11.2020 on the use of rapid antigen tests for the diagnosis of SARS-CoV-2 infection; 2020. https://ec.europa.eu/health/sites/health/files/preparedness_response/docs/sarscov2_rapidantigentests_recommendation_en.pdf
19. European Centre for Disease Prevention and Control. Options for the use of rapid antigen tests for COVID-19 in the EU/EEA and the UK. TECHNICAL REPORT; 2020. https://www.ecdc.europa.eu/en/publications-data/options-use-rapid-antigen-tests-covid-19-eueea-and-uk. Accessed November 21, 2020
20. Candel FJ, Barreiro P, San Román J, et al. Recommendations for use of antigenic tests in the diagnosis of acute SARS-CoV-2 infection in the second pandemic wave: attitude in different clinical settings. *Rev Esp Quimioter*. 2020;33:466-484. https://doi.org/10.37201/req/120.2020

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

How to cite this article: Pérez-García F, Romanyk J, Moya Gutiérrez H, et al. Comparative evaluation of Panbio and SD Biosensor antigen rapid diagnostic tests for COVID-19 diagnosis. *J Med Virol*. 2021;93:5650–5654. https://doi.org/10.1002/jmv.27089