Clinical sensitivity and specificity of three rapid SARS-CoV-2 antigen Tests on a hospitalized patient cohort: Company A, Company B and Beier

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1. Background

Antigen detection of COVID-19 is key to see whether infection has already taken place however whether this also correlate with protection we still do not know. In addition to antigen testing there is big urgency to have validated rapid diagnostic test (RDT) ready to be rolled out if found to be suitably sensitive and specific to test large populations quickly.It should be noted that there are limited data on whether antigen content will be the same in all patients independent of severity of illness. There are countless RDTs developed/in development and offered to diagnostic laboratories. We have used the following criteria to consider inclusion of a RDT in our validation as the capacity of testing and clinical samples are limited:

1. A wide range of diagnostic tests are commercially available for SARS-CoV-2, some of which have received authorizations for use by various national regulatory agencies like CE marking or FDA(EUA)、NMPA approval. Checking r the company qualification can ensure high QC in place.
2. Due to the pandemic situation high and continuous quantities should to be available within a short period eg a week.
3. Manufacturer should provide all paperwork for their validation studies.
4. Manufacturer should provide relevant details about the test details eg antibody or sanple used for a antigen assay.
5. Specificity and sensitivity should be within an acceptable range; and it is important to check on which population the validation was done eg hospitalized patients, ambulant patients. Relevant controls should have been included eg healthy population and other infections with potential differential diagnosis and cross-reactive nature.
6. Right to share and publish data from validation/comparisons should be clarified.

We have selected Savant, OrientGene and Beier tests as they fulfilled most criteria, and were available in big quantities enough to perform validation on a bigger sample set. The products of these three companies are detection reagents for nucleocapsid antigen.

2. Purpose

This study was conducted at Savibio R&D Center between August 3, 2020 to analyze the clinical sensitivity and specificity of the following rapid tests:

1) COVID-19 Antigen Rapid Test Cassette of Company A
2) Novel Coronavirus(2019-nCov) Rapid Test Cassette of Company B
3) COVID-19 Antigen Rapid Test Kit of Beijing Beier Bioengineering Co., Ltd

3. Sample and reagent

□70 Swab samples from PCR confirmed COVID-19 patients and 100 samples with similar symptoms were used in this test at various time point post symptom onset.

1) COVID-19 Antigen Rapid Test Cassette of Company A. of lot 20200815. Expiry date: 20220214

2) Coronavirus Ag Rapid Test Cassette Rapid(Swab) of Company B lot 20200917. Expiry date: 20220316

3) COVID-19 Antigen Rapid Test Kit of Beijing Beier Bioengineering Co., Ltd. lot 20200902; Expiry date: 2022-03-22

Table 1. Sample panel used to validate the sensitivity and specificity of the antibody RDT for COVID-19

Sensitivity				
Country	Sample source	Infection	No. samples	Post symptom onset range
China	RT-PCR confirmed COVID-19	Moderate/Seriously	70	Within 7 days
China	Healthy donors	NA	20	Within 7 days
China	Non-CoV respiratory infections	Adenovirus	5	Within 7 days
		Human Metapneumovirus	5	Within 7 days
		Parainfluenza virus	5	Within 7 days
		Influenza A	10	Within 7 days
		Influenza B	10	Within 7 days
		Enterovirus	5	Within 7 days
		RSV	5	Within 7 days
		Rhinovirus	5	Within 7 days
		Chlamydia pneumoniae	5	Within 7 days
		Mycoplasma pneumoniae	5	Within 7 days
China	Virus culture	hCoV-229E	5	NA
		hCoV-OC43	5	NA
		hCoV-NL63	5	NA
		hCoV-HKU1	5	NA

Equipment:

Disposables including tips for the pipette

Manual pipette

Timer

Personal protective equipment

4. Test principle

The tests were operated according to the test inserts. Samples were collected from COVID-19 suspected patients at Savibio R&D Center for diagnostic purpose and following PCR confirmation.Then collect throat swabs (three throat swabs were taken from each patient) within 7 days for this evaluation. Patients were mostly moderate/seriously ill.Each sample was tested by one test and interpreted by two operators in parallel from hospital.

5. Test results and data analysis

5.1 Various samples showed (false)negative results with the tests compared to RT-PCR results (Table 3, 4, 5)

Possible reasons for the (false)negative results could be:

□The patients were at the very early infection stage, antigen concentration is below the limit of detection of the test.

□Unknown drugs or other interfering substances.

Table 3 Clinical sensitivity/specificity of the Company A test on SARS-CoV-2/other samples collected within 7 days from the symptom onset

Reagents		PCR		Total
		Positive	Negative	
Company A;s Reagents	Positive	61	5	66
	Negative	9	95	104
Total		70	100	170

The sensitivity on samples collected within 7 days from the symptom onset is 87.14% (95%CI: 79.10% to 95.18%) and the specificity is 95.00% (90.65% to 99.35%).

Table 4 Clinical sensitivity/specificity of the Company B test on SARS-CoV-2/other samples collected within 7 days from the symptom onset

Reagents		PCR		Total
		Positive	Negative	
Company B's Reagents	Positive	59	8	67
	Negative	11	92	103
Total		70	100	170

The sensitivity on samples collected within 7 days from the symptom onset is 84.29% (95%CI: 75.55% to 93.03%) and the specificity is 92.00% (86.59% to 97.14%).

Table 5 Clinical sensitivity/specificity of the Beier's test on SARS-CoV-2/other samples collected within 7 days from the symptom onset

Reagents		PCR		Total
		Positive	Negative	
Beier's Reagents	Positive	68	1	69
	Negative	2	99	101
Total		70	100	170

The sensitivity on samples collected within 7 days from the symptom onset is 97.14% (95%CI: 93.14% to 100%) and the specificity is 99.00% (97.02% to 100.00%).

5.2 Positive results broken down by days since symptom onset

Table 6. Results of cumulative positive rate of Company A' Kit

Days Since Symptom Onset	Cumulative RT-PCR Positive (+)	Cumulative Company A'Kit Positive (+)	PPA
1	3	3	100.00%
2	12	12	100.00%
3	21	21	100.00%
4	36	35	97.22%
5	49	46	93.88%
6	59	54	91.53%
7	70	61	87.14%

Table 7. Results of cumulative positive rate of Company B' Kit

Days Since Symptom Onset	Cumulative RT-PCR Positive (+)	Cumulative Company A'Kit Positive (+)	PPA
1	3	3	100.00%
2	12	12	100.00%
3	21	21	100.00%
4	36	35	97.22%
5	49	46	93.88%
6	59	53	89.83%
7	70	59	84.29%

Table 8. Results of cumulative positive rate of Beier' Kit

Days Since Symptom Onset	Cumulative RT-PCR Positive (+)	Cumulative Company A'Kit Positive (+)	PPA
1	3	3	100.00%
2	12	12	100.00%
3	21	21	100.00%
4	36	36	100.00%
5	49	49	100.00%
6	59	59	100.00%
7	70	68	97.14%

6. Conclusion

According to the test results of the 70 Swab samples from PCR confirmed COVID-19 patients and 100 samples with similar symptoms were used in this test at various time point post symptom onset, the sensitivity/specificity of the tests are:

1) COVID-19 Antigen Rapid Test Cassette of Company A.

The sensitivity on samples collected within 7 days from the symptom onset is 87.14% (95%CI: 79.10% to 95.18%) and the specificity is 95.00% (90.65% to 99.35%). False positive began to appear at 4th day Since Symptom Onset.

2) Coronavirus Ag Rapid Test Cassette Rapid(Swab) of Company B

The sensitivity on samples collected within 7 days from the symptom onset is 84.29% (95%CI: 75.55% to 93.03%) and the specificity is 92.00% (86.59% to 97.14%). False positive began to appear at 4th day Since Symptom Onset.

3) COVID-19 Antigen Rapid Test Kit of Beijing Beier Bioengineering Co., Ltd. lot 20200902; Expiry date: 2022-03-22

The sensitivity on samples collected within 7 days from the symptom onset is 97.14% (95%CI: 93.14% to 100%) and the specificity is 99.00% (97.02% to 100.00%). False positive only appear at 7th day Since Symptom Onset.

Compared to RT-PCR, Beier's kit product showed the highest overall sensitivity followed by Company A and Company B. Samples ＜7 days post symptom onset were detected more often.

Caveat of the specificity owing to limited availability of test kits, the validation was limited on this point. The sensitivity of this reagent is ＞90% and the specificity is ＞95%, which meets our requirements.