Development of the CE-marked VITROS® SARS-CoV-2 Antigen Immunoassay: A Viable Test for the Diagnosis of Symptomatic and Asymptomatic Individuals

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Background – Aim

Timely diagnosis of symptomatic and asymptomatic COVID-19 patients is critical for preventing disease transmission and controlling the pandemic. Consequently, Ortho Clinical Diagnostics has developed the VITROS SARS-CoV-2 Antigen (Ag) assay on the high-throughput VITROS XT 7600 and 5600 Integrated Systems and 3600 Immunodiagnostic System. The product claims and performance data discussed herein are relevant to Ortho's VITROS SARS-CoV-2 Antigen assay available in those countries accepting the CE Mark declaration.

Methods

The VITROS SARS-CoV-2 Ag assay is a chemiluminescent immunoassay that qualitatively detects the nucleocapsid proteins of SARS-CoV-2 in upper respiratory specimens from symptomatic and asymptomatic individuals.[1]

The clinical performance in symptomatic COVID-19 patients has been demonstrated using 177 remnant nasopharyngeal specimens with a SARS-CoV-2 reverse transcription polymerase chain reaction (RT-PCR) result. 46 RT-PCR positive samples were from patients who had been experiencing symptoms for 1 to 5 days. 131 RT-PCR negative samples were collected from all-comers and days since symptom onset was documented where applicable. All samples were analyzed for clinical concordance between the VITROS SARS-CoV-2 Ag assay and high sensitivity RT-PCR methods.

The clinical performance in asymptomatic COVID-19 patients has been demonstrated using 50 remnant mid-turbinate specimens with a SARS-CoV-2 reverse transcription polymerase chain reaction (RT-PCR) result. All samples were collected from staff or residents of an adult care facility as part of routine screening and analyzed by RT-PCR. 20 samples were RT-PCR positive and 30 were RT-PCR negative. All samples were analyzed for clinical concordance between the VITROS SARS-CoV-2 Ag assay and high sensitivity RT-PCR methods.

Results

Symptomatic Individuals

The overall agreement was 98.9% (95% CI, 96.0% to 99.9%) with Positive Percent Agreement (PPA) of 97.8% (95% CI, 88.5% to 100%) and Negative Percent Agreement (NPA) of 99.2% (95% CI, 95.8% to 100%). Furthermore, a 100% PPA was achieved in PCR positive samples with cycle threshold (Ct) values <32[1].

VITROS SARS-CoV-2 Antigen Result	RT-PCR Result		
	Detected	Not-Detected	Total
Reactive	45	1	46
Non-Reactive	1	130	131
Total	46	131	177
PPA		97.8% [95% CI: 88.5-100%]	
NPA		99.2% [95% CI: 95.8-100%]	
Overall Agreement		98.9% [95% CI: 96.0-99.9%]	

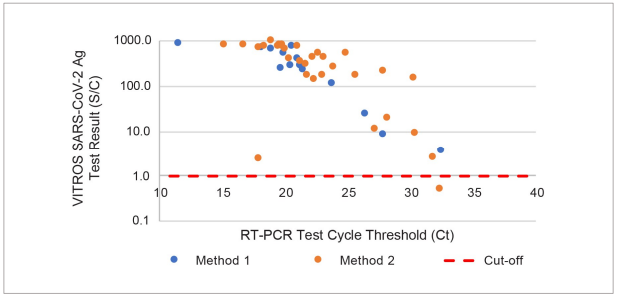
VITROS SARS-CoV-2 Antigen Result	Positive (<32 Ct)	Positive (≥32 Ct)
Reactive	44	1
Non-Reactive	0	1
PPA	100.0%	50.0%
95% CI	92.0-100.0%	1.3 - 98.7%

Results from symptomatic patients were analyzed for percent positive agreement based on the reported days since symptom onset for each patient. The VITROS SARS-CoV-2 Antigen test showed 100% PPA between 1 and 4 days after patients reported symptoms[1].

Days Since Symptom Onset	Cumulative RT-PCR Positive	Cumulative VITROS Reactive	PPA
1	2	2	100.0%
2	6	6	100.0%
3	12	12	100.0%
4	17	17	100.0%
5	46	45	97.8%

Results from symptomatic patients were plotted against the Cycle Threshold from RT-PCR to show correlation based on the amount of virus present in the sample. Two RT-PCR methods were used and VITROS shows strong correlation to the Ct value from each.

VITROS SARS-CoV-2 Ag test results (Signal/Cut-off) vs. RT-PCR Cycle Threshold for symptomatic individuals (days 1–5)[2]



Asymptomatic Individuals

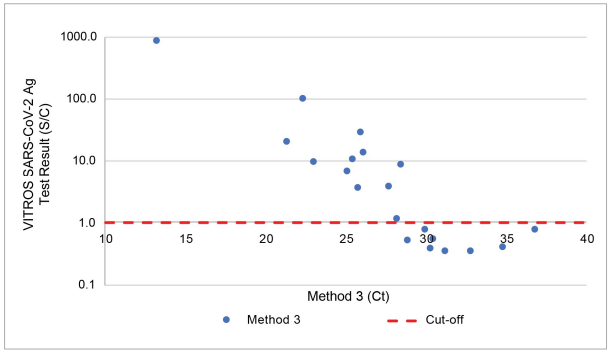
The clinical performance for asymptomatic SARS-CoV-2 carriers has been demonstrated using 50 mid-turbinate nasal specimens retrospectively collected from an adult care facility's staff and residents as part of routine screening and analyzed by RT-PCR. The clinical concordance between the VITROS SARS-CoV-2 Ag assay and RT-PCR was established on all samples and showed a PPA of 92.3% (95% CI, 64.0% to 99.8%) for samples with RT-PCR Ct <30; the NPA was 100%, as all samples with RT-PCR-negative results generated a non-reactive result using the VITROS SARS-CoV-2 Antigen test[1].

VITROS SARS-CoV-2 Antigen Result	RT-PCR		
	Detected	Not Detected	Total
Reactive	12	0	12
Non-Reactive	8	30	38
Total	20	30	50

VITROS SARS-CoV-2 Antigen Result	RT-PCR (<30 Ct)
Reactive	12
Non-Reactive	1
Total	13
PPA	92.3% [95% CI: 64.0-99.8%]

Results from asymptomatic individuals were plotted against the Cycle Threshold values from RT-PCR to show correlation based on the amount of virus present in the sample. One RT-PCR method was used and VITROS shows strong correlation to the Ct value.

VITROS SARS-CoV-2 Ag test results (Signal/Cut-off) vs. RT-PCR Cycle Threshold for asymptomatic individuals[2]



Conclusions

The VITROS SARS-CoV-2 Ag assay demonstrated good clinical sensitivity and specificity in upper respiratory specimens from symptomatic COVID-19 patients as well as from asymptomatic individuals, particularly in samples with RT-PCR Ct <30. Samples with lower RT-PCR Ct values have been associated with higher viral load and are more likely to contain the live virus.

Due to high sensitivity in samples with Ct < 30, a reactive result with the VITROS SARS-CoV-2 Ag test may provide a better indication of infectious status than a reactive result from a qualitative nucleic acid test. Therefore, the VITROS SARS-CoV-2 Ag test is an effective tool in identifying COVID-19 patients who are likely infectious and in controlling SARS-CoV-2 transmission.

References

1) VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Test Instructions for Use. Pub No. GEM1927_XUS-EN, version 2.2.

2) Data on file.

* Product availability subject to local regulatory requirements.

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