

Performance of the BinaxNOW COVID-19 Antigen Rapid Diagnostic Test for the Detection of SARS-CoV-2

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Short report

Keywords: SARS-CoV-2, antigen, RDT, RT-PCR, COVID-19

Posted Date: December 30th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-1206340/v1>

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Abstract

Background: Diagnosis of COVID-19 disease primarily relies on nucleic acid amplification tests (NAAT) that amplify and detect viral RNA in specimens. These methods are expensive and time consuming. Antigen-based rapid diagnostic tests can substantially decrease turnaround time.

Methods: We analyzed paired anterior nares swabs collected from symptomatic patients and asymptomatic healthcare workers being tested COVID-19. One swab was used for a direct RDT and the results were compared to NAAT.

Results: 89 paired specimens were evaluated. The positive percent agreement (PPA) for the antigen RDT was 68.2%, and the negative percent agreement (NPA) was 98.5%. Despite a low PPA, the K statistic was 0.733 indicating substantial agreement with the NAAT result. The median cycle number in paired specimens with concordant results was significantly lower than in discordant specimens (21.3 versus 32.3; $P=0.003$).

Conclusions: The RDT showed modest PPA and high NPA when compared to NAAT. The quick TAT and use of an inexpensive test more frequently could be useful in settings in which results from NAAT testing is delayed.

Introduction

Diagnosis of COVID-19 disease requires a positive molecular test result in which SARS-CoV-2 RNA has been detected [1]. While nucleic acid amplification tests (NAAT) are the preferred, there are multiple pain points, including lack of collection materials, reagents, and consumables for testing, and the amount of time most assays take to complete [2]. Reliance on instrumentation for nucleic acid extraction, amplification, and detection limits accessibility and increases cost. Rapid diagnostic tests (RDTs) have been used—often with mixed results—for other respiratory viral pathogens, including influenza and RSV [3, 4]. Despite a range in sensitivity of RDTs, proponents have suggested that comparing the analytic performance of RDTs to molecular assays is not appropriate [5]. To help slow the spread of SARS-CoV-2, experts have suggested frequent (e.g., daily) testing using RDTs. Modeling studies have suggested that more frequent testing could help curtail ongoing SARS-CoV-2 transmission [6, 7].

The BinaxNOW™ COVID-19 antigen (Abbott Diagnostics Scarborough, Scarborough, ME) is a lateral flow immunoassay that uses antibodies specific to the nucleocapsid protein of SARS-CoV-2 [8]. Herein, we tested paired anterior nares swabs from symptomatic patients and asymptomatic healthcare workers to assess the performance of the RDT COVID-19 antigen test compared to RT-PCR.

Materials And Methods

Paired anterior nares swabs were collected by trained healthcare personnel. Patients were randomly assigned to have either the RDT swab or the RT-PCR swab collected first based on the last digit of the

birth year. One foam-tipped swab (Copan Diagnostics, Murrieta, CA) was used for the BinaxNOW COVID-19 antigen RDT. A certified medical assistant performed the RDT immediately as described in the product insert [8]. A second flocculated swab (Copan) was stored in phosphate buffered saline and transported to the laboratory for RT-PCR testing using Alinity m SARS-CoV-2 assay (Abbott Molecular, Des Plaines, IL) [9]. Samples for RT-PCR were heat inactivated at 65°C for 30 minutes. Molecular testing was performed within 1-8 hours from sample collection. We collected limited demographic and clinical information including age, sex, symptoms and date of symptom onset for each participant. We compared the analytic test performance following guidance from the Clinical and Laboratory Standards Institute [10] when a non-reference test is used as the comparator. Ninety-five percent confidence intervals (CIs) were calculated using the Clopper-Pearson method; Mann Whitney U test was used to compare cycle number (CN) values between groups; p-values <0.05 were considered statistically significant. Analyses were performed using Prism 9 (GraphPad, San Diego, CA). This study was approved by the Rush IRB with a waiver of written consent.

Results

We collected paired samples from 91 patients between November 23 – December 2, 2020. Two antigen RDTs were invalid; the internal control was not visible following the 15 minute incubation, and were excluded from analysis. Forty-six (53%) patients were symptomatic and 43 (47%) patients were asymptomatic. Sixty-six (74%) participants were female, and the median age was 31 years (interquartile range [IQR] 24-38 years). Patient characteristics between groups are presented in Table 1. Among symptomatic participants, the median number of days between symptom onset and sample collection was 3 days (IQR 1-5 days). The most common symptoms reported included cough (63%), runny nose (54%), and headache (54%).

Table 1
Patient characteristics.

Characteristic	Symptomatic (n=46)	Asymptomatic (n=43)
Age, years, median (IQR)	28 (21-37)	33 (29-38)
Sex, % female	32 (70%)	34 (79%)
Days of symptoms before COVID-19 test, median (IQR)	3 (1-5)	N/A
Symptom reported, n(%)		
Fever/chills	18 (39%)	N/A
Cough	29 (63%)	N/A
Shortness of breath	21 (46%)	N/A
Runny nose	25 (54%)	N/A
Sore throat	21 (46%)	N/A
Fatigue	21 (46%)	N/A
Body ache	18 (39%)	N/A
Headache	25 (54%)	N/A
Anosmia	18 (39%)	N/A
Nausea and/or vomiting	15 (32%)	N/A
Diarrhea	11 (24%)	N/A

Overall performance of the RDT is summarized in Table 2. There were 16 (18%) positive RDT results and 73 (80%) negative RDT result. The positive percent agreement (PPA) for the RDT was 68.2% (95% CI, 45.1-86.1) when compared to the SARS-CoV-2 NAAT. The negative percent agreement (NPA) was 98.5% (95% CI, 91.9-99.9). The K statistic was 0.733 (95% CI 0.562-0.904), indicating substantial agreement with the NAAT test based on criteria described by Landis *et al* [11]. Among the 22 NAAT positives patients, 10 had the RDT swab collected first. There was no statistically significant difference in median CN based on the order of swab collection ($P = 0.35$).

Table 2
SARS-CoV-2 test agreement between the antigen RDT and RT-PCR.

BinaxNOW COVID-19 antigen	Abbott Alinity m SARS-CoV-2 NAAT		Kappa ^a (95% CI) ^b
	Detected	Not Detected	
Detected	15	1	0.733 (0.563-0.905)
Not Detected	7	66	
^a Kappa statistical values representing levels of agreement are categorized as follows: < 0, no agreement; 0 to 0.20, slight agreement; 0.21 to 0.40, fair agreement; 0.41 to 0.60, moderate agreement ; 0.60 to 0.80, substantial agreement 0.81 to 1.0 almost perfect agreement.			
^b CI, confidence interval			

Table 3

Symptoms and characteristics of participants providing paired nasal swabs (n=46) for SARS-CoV-2 testing performed using BinaxNOW COVID-19 antigen test and the Alinity m SARS-CoV-2 assay.

Characteristic	True positive (n=15) ^a	False positive (n=1) ^b	False negative (n=6) ^c	True negative (n=24) ^d	Total (n=46)
Fever/chills	7 (47%)	1 (7%)	1 (7%)	9 (50%)	18 (39%)
Cough	10 (34%)	1 (3%)	2 (7%)	16 (55%)	29 (63%)
Shortness of breath	6 (29%)	1 (5%)	3 (14%)	11 (52%)	21 (46%)
Runny nose	9 (36%)	0 (0%)	3 (12%)	13 (52%)	25 (54%)
Sore throat	7 (33%)	1 (5%)	1 (5%)	12 (57%)	21 (46%)
Fatigue	7 (33%)	1 (5%)	1 (5%)	12 (57%)	21 (46%)
Body ache	8 (44%)	1 (5%)	2 (11%)	7 (39%)	18 (39%)
Headache	8 (32%)	1 (4%)	4 (16%)	12 (48%)	25 (54%)
Anosmia	5 (28%)	0 (0%)	4 (22%)	9 (50%)	18 (39%)
Nausea and/or vomiting	4 (27%)	1 (7%)	2 (13%)	8 (53%)	15 (32%)
Diarrhea	1 (9%)	1 (9%)	2 (18%)	7 (64%)	11 (24%)
Testing performed \leq 7 days from symptom onset	15 (35%)	1 (2%)	6 (14%)	21 (49%)	43 (93%)
^a True positive, antigen positive and NAAT positive					
^b False positive, antigen positive and NAAT negative					
^c False negative, antigen negative and NAAT positive					
^d True negative, antigen negative and NAAT negative.					

We identified 8 (9%) samples with discordant results. One symptomatic patient was positive by the RDT with a negative NAAT. Seven patients had negative RDT results but SARS-CoV-2 RNA was detected by NAAT (6/7 were symptomatic). We observed that the CN for specimens that were positive by both RDT

and NAAT were significantly lower (i.e., more viral RNA present) compared to specimens that were positive only by NAAT (median CN 21.3 vs. 32.3; $P = .003$) (**Figure 1A**). For all symptomatic patients, we plotted the CN against the number of days from symptom onset prior to sample collection (**Figure 1B**). We observed discrepancies between RDT and NAAT results when the Alinity CN is greater than 23.

Discussion

The SARS-CoV-2 pandemic continues to spread, largely uncontrolled in some regions. Efforts such as mask wearing and physical distancing have become politicized, rather than simply viewed as mitigation and containment measures to reduce ongoing transmission. Clinical and public health laboratories have faced incredible challenges with sourcing supplies and reagents [12] and staff burnout related to record test volumes. Some experts have suggested using antigen tests for more frequent, less expensive testing at the point-of-care [7].

The BinaxNOW COVID-19 antigen test was granted EUA from the FDA on August 26, 2020, and intended for use in patients within the first 7 days of symptom onset [8]. This lateral flow immunochromatographic assay employs antibodies specific to antigens expressed in the nucleocapsid protein of SARS-CoV-2. Unlike other antigen-based tests, this is read visually and requires no equipment or instrumentation [13]. Reports on the performance characteristics of the BinaxNOW RDT have been mixed. Notably when first released, the RDT had a 97.1% PPA when compared to an EUA RT-PCR assay [8]. Subsequently, the BinaxNOW RDT has also been made available for prescription home use with a self-collected swab, and demonstrated a 91.7% PPA compared to RT-PCR [14]. Since the initial release, the manufacturer has amended the performance characteristics as a result of larger prospective trials. The product insert now indicates a PPA for the RDT is 84.6% compared to RT-PCR.

In our study, we noted a significantly lower PPA of 68% compared to the data reported by the manufacturer. Our findings are similar to others. In one study involving 2,339 healthcare workers, the BinaxNOW had a sensitivity and specificity of 56.6% and 99.9%, respectively [15]. In a sub-group analysis, the reported sensitivity was 83.3% among symptomatic patients. In another study at two community testing sites, the reported overall sensitivity of the RDT was 52.5%, with an increase to 64.2% among symptomatic patients [16]. We had no RDT positives in our asymptomatic healthcare workers, and are unable to make conclusions of its performance. We also identified that RDT results are more likely to be discordant with NAAT results with higher CN. Our observation is consistent with findings from other recent studies [17, 18].

Frequent antigen testing has been suggested as one alternative to identify contagious patients at risk for spreading SARS-CoV-2 [19]. Some suggest samples with high CN or cycle thresholds but negative antigen results are presumably non-infectious. However, there are conflicting data in the literature, and replication-competent virus has been cultured from symptomatic and asymptomatic persons with a range of cycle thresholds as determined by NAAT [16, 20].

Our study does have limitations. First we enrolled a small number participants, therefore our findings may not be generalizable. Second, we did not perform repeat antigen testing in patients with discordant results, therefore we are unable to assess the utility in more frequent antigen testing to identify patients that subsequently develop COVID-19. In conclusion, our results indicate that the BinaxNOW can reliably detects SARS-CoV-2 viral antigens in specimens with high concentrations of viral RNA.

Declarations

Ethics approval: This study was approved by the Rush IRB with a waiver of written informed consent.

Consent for publication: Not applicable.

Availability of data and materials: The datasets during and/or analysed during the current study available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

Funding: This work was completed through internal funding.

Authors' contributions: N.M.M. designed and administered the study. F.O.G. extracted clinical data from the medical record. N.M.M. drafted the manuscript. F.O.G. and N.M.M. analyzed the data. All authors read and approved the final manuscript.

Acknowledgements: The authors acknowledge the clinical employees who collected samples and the laboratory staff that performed PCR testing.

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Figures

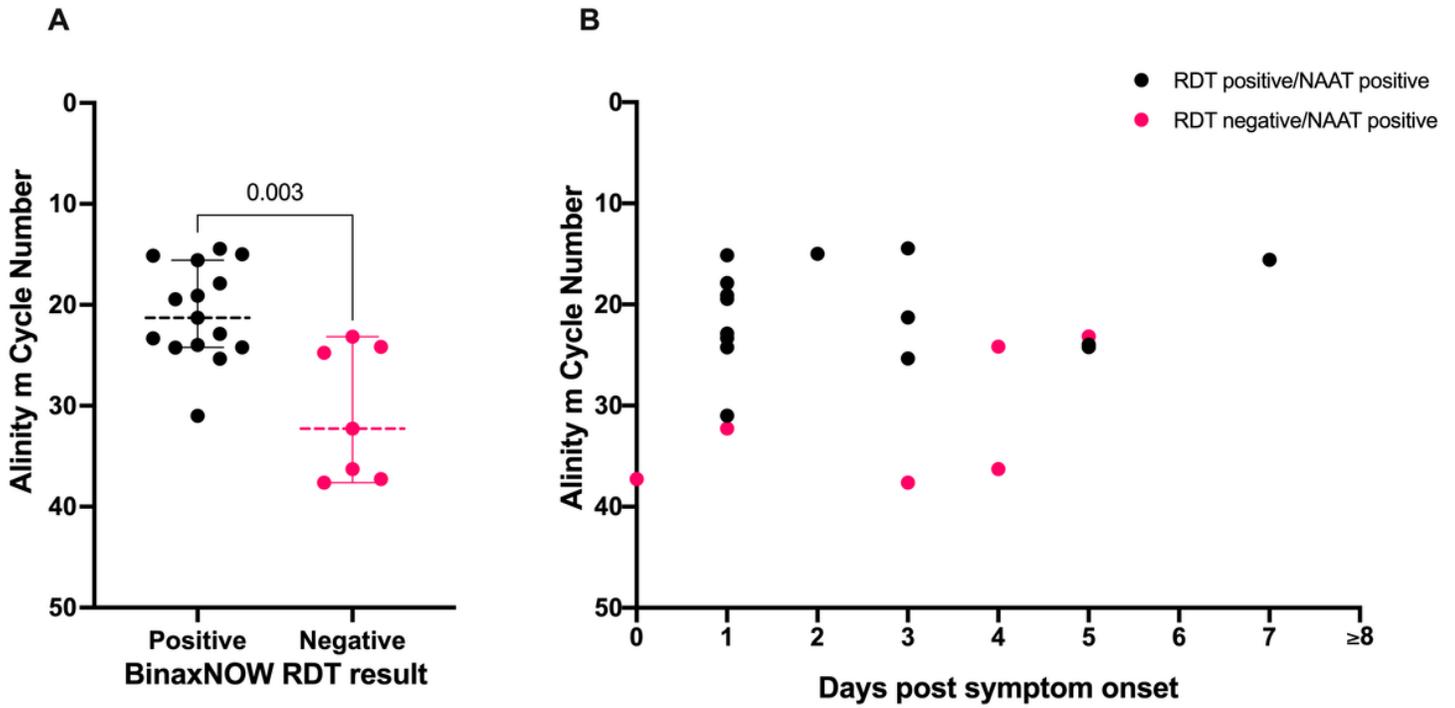


Figure 1

(A) Comparison of median cycle numbers (IQR) measured on the Abbott Alinity m for patients in which both the antigen RDT and NAAT were positive (black circles) vs. antigen RDT negative, NAAT positive specimens (pink circles). (B) Cycle numbers obtained from symptomatic patients are plotted based on the number of days post symptom onset.