Utility of Covid-19 point of care antigen tests in low-middle income settings

UTILITY OF COVID-19 POINT OF CARE ANTIGEN TESTS IN LOW-MIDDLE INCOME SETTINGS

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BACKGROUND

Access to SARS-CoV-2 polymerase chain reaction (PCR) testing is a bottleneck globally, especially in low-and middle-income countries (LMICs). Reliable point-of-care (POC) diagnostics for coronavirus disease 2019 (COVID-19) are cheaper and easier to scale-up than PCR especially in LMICs, and will facilitate interruption of transmission. We report the **field-based performance** of rapid point-of-care (POC) antigen COVID-19 tests **during the beta and delta waves, in South Africa, after laboratory-based validation.**

METHODS

We enrolled symptomatic, ambulatory persons under investigation (PUIs) aged 18 years and older, presenting for SARS-CoV-2 diagnosis at public health facilities in three provinces, South Africa. All patients completed a symptom questionnaire. Nasopharyngeal swabs were taken and processed for SARS-CoV-2 polymerase chain reaction (PCR) testing on either a GeneXpert (Cepheid, USA), Biofire (Biofire, USA) or Cobas (Roche, Switzerland) platform at routine, accredited National Health Laboratory Service laboratories, as per routine national protocols. Concomitantly, trained study staff performed three POC antigen tests at health facilities (Table 1) using a nasal/nasopharyngeal swab, as per manufacturer's recommendations. The sensitivity (S), specificity (Sp), positive (PPV) and negative predictive (NPV) values of tests for PUIs and contacts were calculated using **PCR as the reference standard.**

Table 1: Rapid antigen tests used in this study

Test	Lot number
Rapigen	H073006SD
SD Biosensor Standard Q	QC01020030
LumiraDx	GM2000106, GM2000270

RESULTS

Between Oct 2020-2021, 1696 participants presenting with symptoms of acute COVID-19 (PUIs) were enrolled: 426 (25%) tested PCR positive at baseline; 55% were female; median age was 41 years; 74% were Black African, 7% were living with HIV and 30% were hospitalised (Table 2). Median days since symptom onset was 3 (IQR 2-6). Performance of the three antigen tests ranged from 35-75%, depending on test and days since symptom onset (Tables 3 and 4).

Field based performance of rapid antigen tests ranged from 35-75% sensitivity depending on test and days since symptom onset. Performance was better at the median of 3 days, or more since symptom onset. Further work is needed to understand performance by cycle threshold values, PCR platform, and SARS-CoV.2 variant. Diagnostic algorithms using rapid antigen tests must extend to a PCR in symptomatic individuals with a negative antigen test.

25% PCR positivity

Table 2: Characteristics of study population

Characteristic	Summary
Total at baseline	1696
Total at follow-up	507
Sex assigned at birth, n (%)	
Male	761 (44.9%)
Female	926 (54.6%)
Other/Missing/Unknown	9 (0.6%)
Age (years), median (IQR)	41 (30 – 55)
Ethnicity	
Black African	1261 (74.4%)
Mixed race	242 (14.3%)
Caucasian	126 (7.4%)
Indian	38 (2.2%)
Other/Missing	29 (1.7%)
HIV status	
Negative	1564 (92.2%)
Positive	125 (7.4%)
Unknown	7 (0.4%)
Hospitalisation status	
No	1059 (62.4%)
Yes	513 (30.3%)
Unknown	124 (7.3%)
Number of symptoms	
None	129 (7.6%)
One	213 (12.6%)
Two	294 (17.4%)
Three	248 (14.7%)
Four	186 (11.0%)
At least five	623 (36.8%)
Days symptom onset, median (IQR)	3 (2 – 6)

Table 3: Rapid antigen test performance: Reference: PCR

Point of Care antigen tests*	Sensitivity (95%CI)	Specificity (95%CI)	PPV (95%CI)	NPV (95%CI)
Rapigen (n=277)	35.3 (26.7 – 44.8)	97.5 (93.8 – 99.3)	91.1 (78.8 – 97.5)	67.7 (61.2 – 73.6)
SD Biosensor Ltd (n=768)	51.2 (45.3 – 57.2)	96.5 (94.4 – 97.9)	89.5 (83.7 – 93.8)	77.2 (73.7 – 80.5)
LumiraDx (n=627)	65.5 (57.3 – 73.2)	96.5 (94.4 – 97.9)	85.1 (77.2 – 91.1)	90.1 (87.1 – 92.5)

Table 4: Rapid antigen performance by days since symptom onset: Reference: PCR

Point of Care antigen tests*	Sensitivity (95%CI)	Specificity (95%CI)	PPV (95%CI)	NPV (95%CI)
RAPIGEN (n=277)	35.3 26.7 – 44.8)	97.5 (93.8 – 99.3)	91.1 (78.8 – 97.5)	67.7 (61.2 – 73.6)
Less than 3 days	43.8 (19.8 – 70.1)	100 (80.8 – 100)	100 (59.0 – 100)	65.4 (44.3 – 82.8)
At least 3 days	30.0 (6.7 – 65.2)	94.4 (72.7 – 99.9)	75 (19.4 – 99.4)	70.8 48.9 – 87.4)
SD BIOSENSOR (n=768)	51.2 (45.3 – 57.2)	96.5 (94.4 – 97.9)	89.5 (83.7 – 93.8)	77.2 (73.7 – 80.5)
Less than 3 days	27.3 (10.7 – 50.2)	97.2 (85.5 – 99.9)	85.7 (42.1 – 99.6)	68.6 (54.1 – 80.9)
At least 3 days	53.8 (33.4 – 73.4)	91.8 (80.4 – 97.7)	77.8 (52.4 – 98.6)	78.9 (66.1 – 88.6)
LumiraDx (n=627)	65.5 (57.3 – 73.2)	96.5 (94.4 – 97.9)	85.1 (77.2 – 91.1)	90.1 (87.1 – 92.5)
Less than 3 days	65 (40.8 – 84.6)	96 (86.1 – 99)	81.3 (54.4 – 96)	89.1 (78.7 – 95.5)
At least 3 days	75 (42.8 – 94.5)	100 (92.9 – 100)	100 (65.4 – 100)	94.3 (84.3 – 98.8)

CONCLUSIONS

In a real world setting, during the beta and delta waves, compared with PCR the sensitivity of rapid antigen tests ranged from 35-75% depending on test type and days since symptom onset. At a median of 3-days since symptom onset, performance was better than earlier on (<3 days) in the disease process. Further work is needed to understand rapid antigen test performance by cycle threshold values, by PCR platform, and by SARS-CoV.2 variant. Meanwhile, improved POC diagnostics are needed to facilitate COVID-19 diagnosis in LMICs where PCR is not always accessible.

ADDITIONAL KEY INFORMATION

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