Validating Rapid Point-of-Care Strep A Test Accuracy in Sub-Saharan Africa: Pilot Results from Two Sites

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Introduction

- Rheumatic heart disease (RHD) is a preventable chronic heart condition which evolves from an untreated Group A Streptococcus (Strep A) bacterial infection. Prompt diagnosis of Strep A and treatment with antibiotics can be life-saving.

- Rapid point-of-care (POC) tests have been developed for timely Strep A diagnosis and could prove advantageous given the constraints associated with throat cultures in resource-scarce RHD endemic regions such as Africa.

- In this report, we present two rapid POC Strep A test kits (Sure-Vue™ Signature and BinaxNOW®) used among at-risk populations in Uganda and South Africa, validated against polymerase chain reaction (PCR) and culture results.

Purpose

To test the validity of Western-developed Strep A rapid POC tests within the sub-Saharan Africa context.

Methods

Data Collection

- The South African cohort was recruited over 5 months, from a community clinic in peri-urban Cape Town. A throat swab specimen for culture as well as for the BinaxNOW® rapid test, was taken from consenting participants, not having been on antibiotic treatment in the preceding 14 days. All Strep A isolated from serial throat cultures were grouped and *emm*-typed according to standard protocols.

- The Uganda cohort was recruited from a four-week primary school-based prospective cohort in the Gulu District. During the active surveillance period, all children attending the school were asked to present for evaluation. A history, clinical examination, and swab for culture, PCR, and the Sure-Vue™ Signature rapid test were completed.

Data Analysis

- Data were analysed using RStudio Version 1.2.5019. Median with range were used to summarise non-parametric continuous variables and frequencies with percentages were used to summarise categorical data. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated using standard formulae for the Uganda cohort.

Results

Participant characteristics (table 1) in both samples included slightly more females than males (59% in Gulu, 69% in Cape Town), and similar ages ranging from 6 to 16 years. More than half of the Gulu cohort experienced a cough (57%), which was rarer among the Cape Town cohort (12.5%). Both cohorts experienced similar rates of tonsillar exudates (3.5% in Gulu, 2.1% in Cape Town) and tonsillar swelling (41% in Gulu, 40% in Cape Town).

Table 1: Characteristics of participants at time of presentation for Streptococcus pyogenes Group A testing, stratified by two Sub-Saharan African countries

	City, Country	
	Gulu, Uganda	Cape Town, South Africa
	N = 311	N = 48
Demographics		
Age, years, median (min-max)	11 (6-16)	9 (6-13)
Male	128 (41.2%)	15 (31.2%)
Female	183 (58.8%)	33 (68.8%)
Presenting signs and symptoms		
Abdominal pain	130 (41.8%)	-
Conjunctivitis	5 (1.6%)	0 (0%)
Coryza	108 (34.7%)	-
Cough	178 (57.2%)	6 (12.5%)
Diarrhoea	47 (15.1%)	-
Fever	32 (10.3%)	4 (8.3%)
Headache	140 (48.2%)	-
Rash	-	2 (4.2%)
Rhinorrhoea	-	3 (6.3%)
Tender anterior cervical node	137 (44.1%)	0 (0%)
Tonsillar exudates	11 (3.5%)	1 (2.1%)
Tonsillar swelling	127 (40.8%)	19 (39.6%)

Variable distributions are reported as n (%) unless otherwise specified

- All 48 BinaxNOW® Strep A tests performed in South Africa were negative, of which **five** were found to be positive for Strep A through confirmatory culture. **Emm-types** were available for three of these results (1.0, 2.0, 94.0), while the remaining samples were either not typable or isolates not received.

- Of the Sure-Vue™ signature Strep A tests performed in Gulu 113 (36.3%) were positive; however, a lower positivity among culture 23 (7.4%) and PCR 24 (7.7%) was observed.

- When the Sure-Vue™ signature Strep A test was compared to confirmatory culture, it had a **sensitivity of 48%** and **specificity of 65%**; the **positive predictive value was 10%** and **negative predictive value equalled 95%** (table 2).

Table 2: Sensitivity and specificity analysis of test results for PCR and Rapid Strep Testing in Gulu, Uganda, where culture results are used as the gold standard

	Point estimates and (95% CIs)			
Test (Confirmatory Culture)	**Sensitivity**	**Specificity**	**PPV**	**NPV**
PCR	1.00 (0.85, 1.00)	0.97 (0.87, 1.00)	0.96 (0.79, 1.00)	1.00 (0.91, 1.00)
Rapid Strep (Sure-Vue Strep A Test)	0.48 (0.27, 0.69)	0.65 (0.59, 0.70)	0.10 (0.05, 0.17)	0.94 (0.89, 0.97)

PPV, positive predictive value; NPV, negative predictive value

Discussion

- The manufacturer of Sure-Vue™ signature Strep A test, Fisher Healthcare, reports a 95.7% sensitivity and 100% specificity, which was much higher than 48% and 65% respectively reported in our Uganda cohort.

- Data collection in Cape Town was limited by the COVID-19 pandemic resulting in insufficient data to perform statistical analysis; however, five of the 48 BinaxNOW® Strep A tests were false negative results, as confirmed by culture.

- Had the results of this study validated the use of these rapid POC tests in the African setting, a more accurate diagnosis of Strep A infection and treatment with appropriate and timely antibiotics would be possible.

- Limitations associated with this study include the lack of *emm*-type data and uncertainty around Uganda's laboratory culture results.

Conclusion

This brief report provides evidence that current rapid POC tests for Strep A perform poorly in sub-Saharan Africa, thus necessitating confirmatory testing with culture or PCR. While laboratory reliability could have played a role, these results are likely attributable to regional variation in Strep A genetic markers.

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Literature Cited

Abbott. BinaxNOW® Strep A Test: Product Details [Internet]. 2021 [cited 2021 Apr 12]. Available from: https://www.globalpointofcare.abbott/en/product-details/binaxnow-strep-a.html

DeWyer A, Scheel A, Webel AR, Longenecker CT, Kamarembo J, Aliku T, Engel ME, Bowen AC, Bwanga F, Hovis I, Chang A. Prevalence of group A β-hemolytic streptococcal throat carriage and prospective pilot surveillance of streptococcal sore throat in Ugandan school children. International Journal of Infectious Diseases. 2020 Apr 1;93:245-51.

Fisher Healthcare™. Fisher Healthcare Sure-Vue Kits [Internet]. [cited 2021 Apr 12]. Available from: https://www.fishersci.com/us/en/healthcare-products/selection-guides/fisher-healthcare-sure-vue-kits.html

Karthikeyan G, Mayosi BM. Is primary prevention of rheumatic fever the missing link in the control of rheumatic heart disease in Africa? *Circulation* 2009;120(8):709–13.

Zühlke LJ, Beaton A, Engel ME, Hugo-Hamman CT, Karthikeyan G, Katzenellenbogen JM, et al. Group A Streptococcus, Acute Rheumatic Fever and Rheumatic Heart Disease: Epidemiology and Clinical Considerations. *Curr Treat Options Cardiovasc Med* [Internet] 2017;19(2):15. Available from: http://link.springer.com/10.1007/s11936-017-0513-y