International Journal of Infectious Diseases 14 (2010) e1048–e1053

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

The utility of rapid antigen detection testing for the diagnosis of streptococcal pharyngitis in low-resource settings

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ARTICLE INFO

Article history:
Received 16 October 2009

Corresponding Editor: William Cameron, Ottawa, Canada

Keywords:
Streptococcal infection
Pharyngitis
Rapid diagnostic tests
Clinical signs
International child health

SUMMARY

Objectives: To evaluate the utility of rapid antigen detection testing (RADT) for the diagnosis of group A streptococcal (GAS) pharyngitis in pediatric outpatient clinics in four countries with varied socio-economic and geographic profiles.
Methods: We prospectively evaluated the utility of a commercial RADT in children aged 2–12 years presenting with symptoms of pharyngitis to urban outpatient clinics in Brazil, Croatia, Egypt, and Latvia between August 2001 and December 2005. We compared the performance of the RADT to culture using diagnostic and agreement statistics, including sensitivity, specificity, and positive and negative predictive values. The Centor scores for GAS diagnosis were used to assess the potential effect of spectrum bias on RADT results.
Results: Two thousand four hundred and seventy-two children were enrolled at four sites. The prevalence of GAS by throat culture varied by country (range 24.5–39.4%) and by RADT (range 23.9–41.8%). Compared to culture, RADT sensitivity ranged from 72.4% to 91.8% and specificity ranged from 85.7% to 96.4%. The positive predictive value ranged from 67.9% to 88.6% and negative predictive value ranged from 88.1% to 95.7%.
Conclusions: In limited-resource regions where microbiological diagnosis is not feasible or practical, RADTs should be considered an option that can be performed in a clinic and provide timely results.

1. Introduction

Group A beta-hemolytic streptococcal (GAS) pharyngitis is a common illness in children and the most common bacterial cause of acute pharyngitis worldwide. In affluent countries, the non-suppurative sequelae of untreated GAS pharyngitis including acute rheumatic fever (ARF) and rheumatic heart disease (RHD) are now rare. However, in regions with limited resources, ARF and RHD are still significant causes of morbidity and mortality, with prevalence rates that range from 1 to 5 per 1000 school-aged children, leading to more than 400 000 deaths annually.[1] In these regions microbiological culture diagnosis is often not widely available, and thus most cases of pharyngitis are treated presumptively.

Primary prevention of ARF/RHD is achieved through accurate diagnosis and treatment of GAS infection. Current North American strategies for the diagnosis of GAS incorporate the use of clinical judgment, throat culture and/or rapid antigen tests. The clinical signs and symptoms of GAS and non-GAS pharyngitis overlap broadly and can be non-specific. Clinical prediction algorithms have been evaluated in a variety of settings with limited sensitivity and specificity for use without laboratory confirmation.[2–6] US practice guidelines recommend that for all pharyngitis cases a laboratory test should be performed to determine whether GAS are present in the throat, unless the physician is able to confidently

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doi:10.1016/j.ijid.2010.02.2269

exclude the diagnosis of streptococcal pharyngitis on clinical grounds.[7]

Culture of a throat swab on sheep blood agar medium remains the gold standard for the laboratory diagnosis of GAS pharyngitis.[7–10] However, laboratory infrastructure and the costs and time associated with throat cultures can present limitations for its use as a diagnostic tool in low-resource settings. A major disadvantage of the throat culture is that it takes up to 48 h to obtain a result. In many low-resource settings, the lag period between specimen collection and final microbiological diagnosis is particularly problematic, since it may not be feasible for patients to return for a follow-up visit and appropriate treatment.

In the 1980s, rapid antigen detection tests (RADT) were developed to simplify the diagnosis of GAS.[11] Compared with throat culture, RADTs have a high specificity, ranging from 90% to 99%. The sensitivity of RADTs, however, is variable, depending upon the type of commercial kit used and the study design, ranging from 75% to 95%.[10] This variation in sensitivity has been attributed to differences in disease spectrum among study populations, culture methods, and laboratory performance. Given the variation in reported sensitivity of RADTs, the American Academy of Pediatrics, the Infectious Diseases Society of America, and the American Heart Association continue to recommend confirmation of negative RADT results with throat culture.[7–9,12]

There is currently no international consensus on the use of RADTs for the diagnosis of GAS pharyngitis, however these kits have been widely adopted in Europe and the USA.[13] Despite the variation in sensitivity, there are many advantages to RADTs for the diagnosis of GAS pharyngitis. They are simple to perform both in the laboratory and clinic/office setting and the results are available at the point of care in less than 15 min. Whereas throat cultures require a microbiology laboratory and a return visit to obtain results 1–2 days after initial contact with the patient, RADTs provide rapid diagnosis, which leads to faster, more accurate treatment, a reduction in indiscriminate antibiotic use, and a subsequent reduction in the incidence of the non-suppurative sequelae of untreated GAS pharyngitis.[10] RADTs are generally well characterized, commercially produced to meet uniform standards, and include internal controls for accuracy of diagnosis. For these reasons, in low-resource settings where throat culture is not feasible due to the absence of a laboratory or skilled personnel or lag time associated with obtaining results, RADTs without the recommended culture confirmation may still present a practical alternative to clinical diagnostic algorithms alone.[3]

To assess the utility of RADTs in varied clinical settings, we compared the performance of a commercially available rapid antigen detection test–the STREP A OIA MAX (Thermo Biostar/ Inverness Medical Professional Diagnostics, Princeton, NJ, USA)–with standard throat culture, in Brazil, Croatia, Latvia, and Egypt.[14–17] To our knowledge, this is the first prospective multi-country evaluation of a RADT for GAS pharyngitis using a single standard protocol.

2. Patients and methods

These data were gathered in the context of a multi-country study designed to evaluate signs and symptoms of GAS pharyngitis in children and develop new clinical guidelines for the diagnosis of GAS pharyngitis in low-resource settings where laboratory confirmation is not always readily available. Data from this study describing differences in presentation of GAS pharyngitis have been published elsewhere.[4,18]

From August 2001 through December 2005, children aged 2–12 years presenting to participating clinics with a complaint of sore throat were consecutively enrolled in four urban pediatric outpatient clinics in Rio de Janeiro, Brazil; Zagreb, Croatia; Cairo, Egypt; and Riga, Latvia. A child was excluded if the parent/guardian reported oral antibiotic use in the three days prior to screening or parenteral antibiotic use in the 28 days before screening, if there was a history of rheumatic fever or RHD, or if the child required hospitalization for any reason at the time of enrollment. All study sites used a common study protocol and data collection forms. All data collection forms were translated into the local language.

The study protocol was approved by both local and national institutional review boards at each of the clinical sites, the World Health Organization (WHO) in Geneva, and the Committee on Human Research at the Johns Hopkins Bloomberg School of Public Health. Informed consent was obtained from the parent or guardian accompanying the child to the clinic and child assent was obtained from all children aged 5 years or older.

After patients were enrolled in the study, a physical examination was performed and demographic and clinical data were collected. Two throat swabs were taken simultaneously from each patient for both culture and rapid antigen assay using sterile cotton-tipped swabs. Throat culture specimens were plated on 5% sheep blood agar and incubated anaerobically at 37.0 °C; plates were examined at 24 and 48 h for the presence of β-hemolytic streptococci, with confirmation by bacitracin disk.[19] Laboratory staff at each site were trained using the WHO manual *Laboratory diagnosis for group A streptococcal infections*.[19] All sites were provided with uniform training to ensure uniform laboratory procedures for both throat culture and rapid tests. Regular site visits were made to each participating laboratory to ensure that standard methods were being used. The RADT was performed by trained study personnel according to the instructions in the manufacturer's package insert. The RADT has internal positive and negative controls and has a reported sensitivity range of 79.5–98.1% and specificity of 96.9–99.0%, compared to throat culture.[15–17,20,21]

2.1. Statistical methods

Patient demographic and clinical characteristics were compared using Student's *t*-tests for continuous variables and Chi-square analysis for categorical variables. RADT results were assessed for performance against throat culture results within each study site using the following diagnostic and agreement statistics: sensitivity, specificity, positive and negative predictive values, and diagnostic odds ratio.[22] The sensitivity and specificity of the RADT for the detection of GAS pharyngitis were compared among study sites using Chi-square tests with $\alpha = 0.05$ criterion of significance. Spectrum bias was evaluated by comparing the performance of the RADT in relationship to disease severity. The Centor criteria (history of fever, absence of cough, pharyngeal or tonsillar exudates, and cervical lymphadenopathy) were used to define the clinical spectrum of acute pharyngitis.[23] The Centor score was defined as the number of criteria present, ranging from zero to four. Sensitivity and negative predictive values of the RADT test were calculated on the basis of Centor scores at each study site. We conducted a Cuzick nonparametric trend test within each site to compare the sensitivity of the RADT test across sites with increasing Centor scores. Statistical significance was accepted at $p \leq 0.05$, two-tailed. Analyses were carried out with STATA statistical software, version 10.0.[24]

3. Results

A total of 2598 children were enrolled in the study (Brazil $n = 294$, Croatia $n = 404$, Egypt $n = 1642$, Latvia $n = 258$). One hundred and twenty-six subjects (110 in Brazil and 16 in Egypt) were excluded from the analyses due to missing laboratory data, resulting in a final sample size of 2472 for analysis. A larger number of patients were recruited from the Egypt site compared to

Table 1
Comparisons of clinical and demographic characteristics by country

	All sites	Brazil	Croatia	Egypt	Latvia
Total number of patients	2472	184	404	1626	258
Age (years), mean ± SD	5.2 ± 0.05	5.8 ± 0.21	5.8 ± 0.14	4.8 ± 0.06	6.6 ± 1.9
Gender female, *n* (%)	1070 (43.3)	95 (51.6)	169 (41.8)	687 (42.3)	119 (46.1)
Clinical characteristics, *n* (%)					
History of fever	1997 (80.8)	162 (88.0)	257 (63.6)	1348 (82.9)	230 (89.1)
Absence of cough	1037 (41.9)	80 (43.5)	239 (59.2)	540 (33.2)	178 (69.0)
Pharyngeal or tonsillar exudates	753 (30.5)	52 (28.3)	155 (38.4)	385 (23.7)	161 (62.4)
Cervical lymphadenopathy	686 (27.8)	52 (28.3)	158 (39.1)	291 (17.9)	185 (71.7)

SD, standard deviation.

the other sites due to the large size of the outpatient clinic and the experience of the local staff in conducting large clinical studies. Each study site enrolled patients for at least one full calendar year.

Patient demographic and clinical characteristics varied across study sites and are shown in Table 1. The mean age of patients across sites ranged from 4.8 years in Egypt to 6.6 years in Latvia ($p < 0.001$).

Table 2 presents microbiological findings and the performance measures of the RADT as compared to throat culture at each study site. The proportion of children with a positive GAS throat culture ranged from 24.5% in Brazil to 39.4% in Croatia ($p < 0.001$). Positive RADT results also varied by country, ranging from 23.9% in Brazil to 41.8% in Croatia. Concordance between the two test results in the same patient ranged from 81.8% to 94.0% and discordance ranged from 5.9% to 18.2%. The sensitivity of the RADT ranged from 72.4% in Latvia to 91.8% in Croatia and the specificity ranged from 85.7% in Latvia to 96.4% in Brazil. The positive predictive value and negative predictive value were highest in Brazil (88.6% and 95.7%, respectively) and lowest in Latvia (67.9% and 88.1%, respectively). The diagnostic odds ratio was highest in Brazil.

Table 2
Comparisons of microbiological findings among countries

	Brazil (*n* = 184)	Croatia (*n* = 404)	Egypt (*n* = 1626)	Latvia (*n* = 258)
GAS prevalence, *n* (%)				
Positive OIA MAX	44 (23.9)	169 (41.8)	403 (24.8)	81 (31.4)
Positive throat culture	45 (24.5)	159 (39.4)	430 (26.4)	76 (29.5)
Discordance,[a] *n* (%)				
Positive OIA MAX/negative culture	5 (2.7)	23 (5.7)	82 (5.0)	26 (10.1)
Negative OIA MAX/positive culture	6 (3.3)	13 (3.2)	109 (6.7)	21 (8.1)
Concordance,[b] *n* (%)				
Positive OIA MAX/positive culture	39 (21.2)	146 (36.1)	321 (19.7)	55 (21.3)
Negative OIA MAX/negative culture	134 (72.8)	222 (55.0)	1114 (68.5)	156 (60.5)
OIA MAX performance (95% CI)				
Sensitivity	86.7 (73.2–94.9)	91.8 (86.4–95.6)	74.7 (70.3–78.7)	72.4 (60.9–82.0)
Specificity	96.4 (91.8–98.8)	90.6 (86.2–94.0)	93.1 (91.6–94.5)	85.7 (79.8–90.5)
PPV	88.6 (75.4–96.2)	86.4 (80.3–91.2)	79.7 (75.4–83.5)	67.9 (56.6–77.8)
NPV	95.7 (90.9–98.4)	94.5 (90.7–97.7)	91.1 (89.3–92.6)	88.1 (82.4–92.5)
Diagnostic odds ratio	3.33	0.89	2.97	3.10

OIA MAX, STREP A OIA MAX test; PPV, positive predictive value; NPV, negative predictive value; CI, confidence interval; RADT, rapid antigen detection test.
[a] The results of RADT and cultures were discordant in the same patient.
[b] The results of RADT and cultures were concordant in the same patient.

Table 3
Association between clinical factors and detection of GAS pharyngitis by culture or RADT

	n	GAS prevalence (culture)	GAS prevalence (OIA MAX)
Brazil			
History of fever	162	41 (25.3)	42 (25.9)
Absence of cough	80	30 (37.5)[a]	33 (41.2)[a]
Pharyngeal or tonsillar exudates	52	24 (46.2)[a]	25 (48.1)
Cervical lymphadenopathy	52	26 (50)[a]	23 (44.2)[a]
Croatia			
History of fever	257	94 (36.6)	101 (39.3)
Absence of cough	239	110 (46.0)[a]	111 (46.4)[a]
Pharyngeal or tonsillar exudates	155	62 (40)	69 (44.5)
Cervical lymphadenopathy	156	76 (48.7)[a]	79 (50.6)[a]
Egypt			
History of fever	1348	361 (26.8)	341 (25.3)
Absence of cough	540	430 (79.6)[a]	173 (32.0)[a]
Pharyngeal or tonsillar exudates	385	121 (31.4)[a]	123 (31.9)[a]
Cervical lymphadenopathy	291	96 (33.0)[a]	106 (36.4)[a]
Latvia			
History of fever	230	67 (29.1)	73 (31.7)
Absence of cough	178	51 (28.7)	57 (32.0)
Pharyngeal or tonsillar exudates	161	48 (29.8)	47 (29.2)
Cervical lymphadenopathy	185	59 (31.9)[a]	59 (31.9)

GAS, group A Streptococcus; RADT, rapid antigen detection test; OIA MAX, STREP A OIA MAX test.
Results are *n* (%).
[a] Statistically significant, $p \leq 0.05$.

Table 4
Sensitivity and negative predictive values of RADT as stratified by the Centor criteria scores[a]

	Centor score				
	0	1	2	3	4
Brazil (n = 184)					
No. of patients (% total)	10 (5.4)	68 (37.0)	58 (31.5)	30 (16.3)	18 (9.8)
Positive OIA MAX, n (%)	0 (0)	5 (7.3)	11 (19.0)	16 (53.3)	12 (66.7)
Positive cultures, n (%)	0 (0)	7 (10.3)	12 (20.7)	14 (46.7)	12 (66.7)
Sensitivity, % (95% CI)	–	42.9 (9.9–81.6)	83.3 (51.6–97.9)	100 (76.8–100)	100 (73.5–100)
NPV, % (95% CI)	–	93.7 (84.5–98.2)	95.7 (85.5–99.5)	100 (76.8–100)	100 (54.1–100)
Croatia (n = 404)					
No. of patients (%)	28 (6.9)	98 (24.3)	151 (37.4)	101 (25)	26 (6.4)
Positive OIA MAX, n (%)	10 (35.7)	34 (34.7)	64 (42.4)	46 (45.5)	15 (57.7)
Positive cultures, n (%)	8 (28.6)	29 (29.6)	66 (43.7)	43 (42.6)	13 (50)
Sensitivity, % (95% CI)	100 (63.1–100)	93.1 (77.2–99.2)	87.9 (77.5–94.6)	93.0 (80.9–98.5)	100 (75.3–100)
NPV, % (95% CI)	100 (81.5–100)	89.9 (80.2–95.8)	90.8 (82.7–95.9)	94.5 (84.9–98.9)	100 (71.5–100)
Egypt (n = 1626)					
No. of patients (%)	138 (8.5)	725 (44.6)	504 (31.0)	205 (12.6)	54 (3.3)
Positive OIA MAX, n (%)	25 (18.1)	142 (19.6)	134 (26.6)	75 (36.6)	27 (50)
Positive cultures, n (%)	29 (21.0)	164 (22.6)	364 (72.2)	80 (39.0)	18 (33.3)
Sensitivity, % (95% CI)	69.0 (49.2–84.7)	72.0 (64.4–78.7)	73.4 (65.2–80.5)	80.0 (69.6–88.1)	94.4 (72.7–99.9)
NPV, % (95% CI)	92.0 (85.4–96.3)	92.1 (89.6–94.2)	90.0 (86.4–92.8)	87.7 (80.8–92.8)	96.3 (81.0–99.9)
Latvia (n = 258)					
No. of patients (%)	3 (1.2)	34 (13.2)	95 (36.8)	112 (43.4)	14 (5.4)
Positive OIA MAX, n (%)	1 (33.3)	8 (23.5)	33 (34.7)	36 (32.1)	3 (21.4)
Positive cultures, n (%)	1 (33.3)	9 (26.5)	28 (29.5)	34 (30.4)	4 (28.6)
Sensitivity, % (95% CI)	100 (2.5–100)	55.6 (21.2–86.3)	78.6 (59.0–91.7)	70.6 (52.5–84.9)	75 (19.4–99.4)
NPV, % (95% CI)	100 (15.8–100)	84.6 (65.1–95.6)	90.3 (80.1–96.4)	86.8 (77.1–93.5)	90.9 (58.7–99.8)

RADT, rapid antigen detection test; OIA MAX, STREP A OIA MAX test; NPV, negative predictive value; CI, confidence interval.
[a] Centor criteria are history of fever, absence of cough, presence of pharyngeal or tonsillar exudates, and presence of cervical lymphadenopathy.

There were statistically significant differences in the frequency of signs and symptoms associated with clinical presentation of pharyngitis between countries (Table 3). Cervical lymphadenopathy was the only sign that was consistently statistically associated with positive GAS culture at all sites. We did not find a statistical association between the severity of symptoms (based on Centor scores) and RADT sensitivity at any of the participating sites (Brazil $p = 0.1$, Croatia $p = 0.166$, Egypt $p = 0.083$, Latvia $p = 0.488$), as shown in Table 4.

4. Discussion

RADTs have been widely evaluated in various clinical settings, however standardized data from low-resource settings are scant. This study is the first multi-country evaluation of the utility of RADTs for Streptococcus, using a single test and standard protocol at all sites. Previous evaluations of the OIA MAX test in the USA have demonstrated a range of sensitivity from 79.3% to 94.7% and specificity from 96.3% to 100%.[15,25–29] Our study demonstrated a range of sensitivity from 72.4% to 91.8% and specificity from 85.7% to 96.4%. The high negative predictive value in all countries suggests that a negative test would be useful to rule out GAS pharyngitis and potentially reduce unnecessary antibiotic treatment. The diagnostic odds ratio was highest in Brazil (3.33) and lowest in Croatia (0.89). The Croatian diagnostic odds ratio was less than 1, which is atypical, but occurs when the sensitivity is higher than the specificity.

Recent studies have reported that the sensitivity of RADTs may be affected by variation in the spectrum of clinical disease severity or presentation.[30–32] The sensitivity of RADTs has been reported to range from 47% to 65% when applied to patients with a low probability of GAS pharyngitis based on clinical findings. As the probability of GAS pharyngitis increases (based on the number of clinical criteria present), so does the sensitivity of the RADT.[30,31,33,34] This spectrum bias was not observed in our study. We found no statistically significant association between the RADT sensitivity and the spectrum of clinical presentation based on the Centor criteria at any single site or at all sites combined.[35] These data are consistent with a recent study of the same RADT in a US population.[33]

Throat cultures are currently considered the gold standard for diagnosis of GAS pharyngitis; however in settings with limited resources and higher incidences of post-streptococcal cardiac sequelae, as in many economically developing regions, bacterial culture is neither available nor feasible. In these regions, clinicians currently have the choice of treating everyone, treating no one, or utilizing clinical guidelines/rules, which have been shown to vary widely in terms of sensitivity and specificity by region and are subject to the clinical interpretation of nonspecific signs and symptoms.[2–5,18] Current US guidelines recommend confirmation of negative rapid antigen test results with a throat culture, which is considered to have better sensitivity than rapid tests. In our study of more than 2400 children, only a small percentage of patients (3.2–8.1%) were misclassified as GAS-negative by RADT as compared to the local throat culture, which represents the GAS-positive cases that would have been missed without the recommended confirmatory throat culture and may be at risk of the suppurative sequelae of untreated GAS. Misclassification of individuals who were identified as GAS-positive by RADT and GAS-negative by throat culture was also minimal, ranging from 2.7% to 10.1% across sites. These cases represent the individuals who would be 'unnecessarily-treated' using the RADT as compared to throat culture. It is notable that the stratification by Centor scores demonstrated a similar range of misclassification for those individuals who were RADT-negative/throat culture-positive, though the RADT still performed slightly better at each site; however the misclassification of individuals who were RADT-positive/throat culture-negative was consistently high for all sites, with over-treating of up to 60% of patients who did not need antibiotics by local culture criteria.

Cost–benefit analyses have demonstrated that treating all patients with pharyngitis without microbiological confirmation (RADT or culture) would prevent up to 90% of the potential complications related to RHD, which may require costly surgical interventions.[36] Although a treat-everyone strategy is common, and may reduce the incidence of RHD, there will be substantial

unnecessary use of antibiotics. Indiscriminate use of antibiotics may result in unnecessary adverse reactions, increased antibiotic resistance in both Streptococcus and other upper airway organisms, and therefore increased healthcare costs. RADTs may provide significant cost–benefit advantages if the test sensitivity is adequately high.[36–38] In the USA, as at our participating sites, the cost of a RADT (US$5–10) is somewhat lower than the cost of a throat culture (US$15–20).[39] For example, in Brazil a throat culture is approximately US$5.55 whereas a RADT is US$2.77 (personal communication A.L. da Cunha). In Latvia, throat cultures cost US$12.66 as compared to US$4.49 for RADT (personal communication D. Gardovska).

There were several limitations to our study. First, this particular commercial RADT has recently been discontinued in the USA and is no longer available. However, the principle of assessing the utility of any RADT would be similar, as would be the logic for using a RADT with similar performance characteristics in clinics in limited-resource settings. Second, the microbiological culture results may not have been comparable since they were performed in a variety of laboratories in different countries. Throat culture performance is affected by a number of factors including: swab technique, the skill of the personnel who process and interpret blood agar plate cultures, the skill and experience of the laboratory, and the specific materials and conditions used for plating and incubation of the cultures.[20,40] Discordance between the results of simultaneous cultures in the same laboratory is well described in the literature.[32] Assessment of RADT performance is affected by the same issues that affect culture results, however many RADT tests are easier to perform and have internal controls, which minimizes errors. Third, the observed differences in clinical presentation between sites could reflect a selection bias during the recruitment process, differences in access to care, or the parental threshold for care-seeking at each site. To minimize bias and differences in site performance, we provided uniform training and standardized manuals and conducted multiple site visits. Fourth, it is likely that some of the individuals enrolled in our study were carriers rather than acutely infected with GAS. Neither conventional throat culture nor RADTs can differentiate acute GAS pharyngitis from GAS carriers with intercurrent viral pharyngitis. The comparison is valid and a positive result with either test is accepted as a presumptive criterion for treatment for GAS infection.[10] Finally, we were not able to compare sensitivity and specificity of the RADT directly with the sensitivity and specificity of the throat culture across all four countries, as we did not have a third gold standard test (such as a single reference laboratory processing of all throat cultures). However, we did compare the two tests within each country.

5. Conclusions

Given the lower sensitivity of RADTs as compared to throat culture, the current US recommended practice of conducting throat culture confirmation following negative RADT results should be maintained in settings where the resources to perform bacteriological diagnosis are available, return rates for results are high, and appropriate treatment is likely. Nonetheless, the present evaluation suggests that RADTs may have utility in a variety of low- and middle-income country settings. In low-resource settings where laboratory testing is not available, RADTs may be the only feasible solution for rapid, standardized diagnosis of GAS. RADTs may provide quick and accurate diagnosis in lower-level healthcare centers, thus eliminating the need for referrals to higher-level clinics or costly return visits to access test results. In many communities where distances to the closest health facilities are great, healthcare providers are often limited to a single point of contact with the patient to ensure proper treatment.

Our study results suggest that in settings where throat cultures are not feasible, the use of RADTs may provide a reasonable alternative to over-prescription of antibiotics to all children who present with clinical sore throat and a significant improvement over using clinical prediction algorithms for standardized diagnosis. Since RADTs require little or no laboratory infrastructure and can provide rapid results, an affordable RADT that could be used in resource-limited settings should be developed as an important tool to reduce the burden of rheumatic fever and rheumatic heart disease. Cost effectiveness studies are needed to evaluate the cost–benefit of introducing RADTs into resource-limited settings, compared to investing in laboratories for throat cultures or the cost of universal antibiotic treatment for sore throat, or chronic rheumatic heart disease care.

Additionally, these data suggest that a RADT may be useful as an independent standard in select circumstances. GAS pharyngitis results obtained from a throat culture will be influenced by the technique of obtaining the throat swab, the swab used, and variation in microbiology laboratory culture media and procedures, all of which will vary in different settings.[41] Although RADT results may also be subject to variation in the technique used to obtain the throat swabs, RADTs are likely to have less variance due to standardized commercial production and internal controls in the kit. This may be especially beneficial in multi-site clinical studies of GAS pharyngitis, for which standardization is logistically difficult.

Acknowledgements

This study was supported by USAID. The Croatian and Latvian sites were funded by the Department of Child and Adolescent Health and Development, World Health Organization, Geneva. The authors alone are responsible for the views expressed in this publication and they do not necessarily represent the decisions or the stated policy of the World Health Organization. Thermo Biostar donated the STREP A OIA MAX rapid test kits for use in this study free of charge.

Conflict of interest: No conflict of interest to declare.

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