Comparison of the diagnostic accuracy of a rapid immunochromatographic test and the rapid plasma reagin test for antenatal syphilis screening in Mozambique

Pablo J Montoya,[a] Sheila A Lukehart,[b] Paula E Brentlinger,[c] Ana J Blanco,[a] Florencia Floriano,[a] Josefa Sairosse,[d] & Stephen Gloyd[c]

Objective Programmes to control syphilis in developing countries are hampered by a lack of laboratory services, delayed diagnosis, and doubts about current screening methods. We aimed to compare the diagnostic accuracy of an immunochromatographic strip (ICS) test and the rapid plasma reagin (RPR) test with the combined gold standard (RPR, *Treponema pallidum* haemagglutination assay and direct immunofluorescence stain done at a reference laboratory) for the detection of syphilis in pregnancy.
Methods We included test results from 4789 women attending their first antenatal visit at one of six health facilities in Sofala Province, central Mozambique. We compared diagnostic accuracy (sensitivity, specificity, and positive and negative predictive values) of ICS and RPR done at the health facilities and ICS performed at the reference laboratory. We also made subgroup comparisons by human immunodeficiency virus (HIV) and malaria status.
Findings For active syphilis, the sensitivity of the ICS was 95.3% at the reference laboratory, and 84.1% at the health facility. The sensitivity of the RPR at the health facility was 70.7%. Specificity and positive and negative predictive values showed a similar pattern. The ICS outperformed RPR in all comparisons ($P<0.001$).
Conclusion The diagnostic accuracy of the ICS compared favourably with that of the gold standard. The use of the ICS in Mozambique and similar settings may improve the diagnosis of syphilis in health facilities, both with and without laboratories.

Keywords Syphilis serodiagnosis; Prenatal diagnosis; Mozambique (*source: MeSH, NLM*).
Mots clés Séro-diagnostic syphilis; Diagnostic prénatal; Mozambique (*source: MeSH, INSERM*).
Palabras clave Serodiagnóstico de la sífilis; Diagnóstico prenatal; Mozambique (*fuente: DeCS, BIREME*).

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يمكن الاطلاع على الملخص بالعربية في صفحة **103**.

Introduction

Syphilis is an important cause of perinatal morbidity and mortality in resource poor settings. Adverse infant or fetal outcomes arise in 50–80% of pregnancies that survive beyond 12 weeks of gestation,[1–3] especially if pregnancy coincides with the early stages of infection.[4–6] Syphilis is also a substantial cause of adult morbidity and might increase the risk of human immunodeficiency virus (HIV) transmission.[7, 8]

Syphilis control is facilitated by the availability of inexpensive and sensitive diagnostic tests and effective and affordable treatment.[7, 9–12] Antenatal screening and treatment for the disease is highly cost-effective as a means to reduce fetal and infant morbidity and mortality,[13] and furthermore, such measures could contribute to reduced HIV transmission.[8, 14]

Every year, about 1.6 million pregnant women with syphilis remain undiagnosed in sub-Saharan Africa, including more than one million attending antenatal care.[15] Syphilis — as diagnosed by a positive rapid plasma reagin (RPR) test — at the first antenatal visit in Mozambique has a prevalence of about 10% for the country as a whole and 15% for Sofala Province, where our study was conducted.[16]

Scarcity of laboratory services, staff, and training as well as late diagnosis and treatment have hampered efforts to prevent congenital syphilis in Mozambique.[17–19] Furthermore, doubts have also been raised about the accuracy of the currently used syphilis screening tests, such as the RPR, especially in populations with a high prevalence of HIV[20] and malaria.[21]

The recent introduction of rapid immunochromatographic strip (ICS) to screen for treponemal infection would allow syphilis to be both diagnosed and treated in a single visit.[22, 23] Antenatal clinic nurses can do the ICS test in health facilities without a laboratory. Unlike RPR reagents, the ICS can be stored at room temperature and does not require special procedures. A price reduction to

[a] Health Alliance International, PO Box 23, Maputo, Mozambique. Correspondence to Dr Montoya (email: pablom@teledata.mz).
[b] Departments of Medicine/Infectious Diseases, Pathobiology, Microbiology, Periodontics. University of Washington, Seattle, WA, USA.
[c] International Health Program, Department of Health Services. University of Washington, Seattle, WA, USA.
[d] Ministry of Health of Mozambique, Predio de governo 4o andar, Repartição de Asistencia Médica, Direcção provincial de Saúde de Sofala. Beira, Mozambique.
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less than US$ 0.50 per test makes ICS a feasible option for use in settings with scarce resources.

In this study, we aimed to: 1) compare the diagnostic accuracy[24] of ICS and the RPR with a composite gold standard for the detection of syphilis in pregnancy (*Treponema pallidum* haemagglutination assay (TPHA), RPR and direct immunofluorescence stain done at a reference laboratory); 2) compare diagnostic accuracy of ICS and RPR in women with and without HIV or malaria; 3) compare results from the reference laboratory with those from field tests; and 4) describe operational issues that affect the diagnostic accuracy of the tests done in health facilities.

Materials and methods

We recruited participants from a population of pregnant women attending their first antenatal visit at one of six typical health facilities in Sofala Province, Mozambique. We chose health facilities that had a laboratory, that were in a region with high prevalence of syphilis, HIV and malaria, and that had a high number of antenatal patients. Infrastructure at the health facilities was basic and unlike the reference laboratory, buildings at the health facilities did not have air conditioning. Mozambique Ministry of Health staff at the six facilities received 3 days' training on the study and laboratory procedures.

After providing written informed consent, participants answered a questionnaire that included questions about their obstetric and syphilis history. They had an expanded physical examination, which included a search for mucocutaneous lesions suggestive of syphilis, and they provided capillary and venous blood samples.

Staff at the antenatal clinic collected 20 µl of capillary blood with EDTA or non-EDTA capillary tubes from a finger puncture for the SD BioLine Syphilis 3.0 ICS test (Standard Diagnostics Inc., Republic of Korea). An additional blood drop from the same finger prick was taken for a thick blood smear to detect malaria.

Serum from a 5 ml venous blood sample was used for the RPR at the health facilities and the ICS, RPR and TPHA tests (RPR and TPHA from Neomedic Ltd, Healthease, Sea Cow Lake, South Africa) at the Beira Central Hospital reference laboratory (Fig. 1).

We used a solid phase treponemal immunochromatographic assay that provides qualitative detection of antibodies directed towards three *T. pallidum* recombinant antigens; results are obtained after 5–20 minutes. We chose the RPR as our comparison test because it is widely used in syphilis screening.[6, 9, 25–29]

Samples of genital mucocutaneous lesions were smeared on glass slides and sent to the University of Washington, Seattle, WA, USA to be tested with use of direct immunofluorescence stain for *T. pallidum* (ViroStat, Portland, ME, USA). All tests were done in accordance with manufacturers' recommendations. Frequent supervision and assessment took place to ensure valid and reliable results.

Nurses at the antenatal clinics did the initial ICS (hereinafter ICS_{HF}) during the patient's visit. At the health facilities, a laboratory technician who was unaware of the results of the ICS_{HF} did a first qualitative RPR test (hereinafter RPR_{HF}).

At the reference laboratory, technicians who were unaware of the results of previous tests repeated the ICS and RPR tests using serum and the same kit lots as were used at the health facility (hereinafter ICS_{Ref} and RPR_{Ref}). The TPHA was performed as a confirmatory test, and a quantitative RPR was done on serum that had any degree of reactivity in the treponemal (ICS and TPHA) and non-treponemal (RPR) tests.

At the Beira reference laboratory, thick blood smears were stained and read quantitatively for malaria (parasite count per 500 leukocytes adjusted for a presumed leukocyte count of 8000 per µl).

The syphilis status of each participant was defined by a gold standard composed of the TPHA and RPR_{Ref}, and a direct immunofluorescence stain. Possible combinations were: "no syphilis" for TPHA-negative/RPR-negative results; "active syphilis" for TPHA-positive/RPR-positive results; "old or treated syphilis" for TPHA-positive/RPR-negative results, and biological false-positive for TPHA-negative/RPR-positive results. Patients with positive immunofluorescence stain for *T. pallidum* specimens were diagnosed with primary syphilis, irrespective of other laboratory results. All participants with a positive TPHA test result were included in the "all syphilis" serological status group, irrespective of the RPR result.

Data about HIV status were obtained from patients who underwent voluntary counselling and testing for HIV infection as part of routine antenatal care. HIV-positive patients were referred to specialized HIV clinics, as is the normal procedure in Mozambique.

Syphilis was treated with benzathine penicillin and malaria with sulfadoxine-pyrimethamine or chloroquine, dependant on gestational age and in accordance with the clinical protocols of the Mozambique Ministry of Health.[30, 31]

Data were analysed with Stata 7.0. We assumed that with a sample size of 4000 women, we would obtain a precision standard error (SE) of ±3% for the diagnosis of active syphilis. We compared the performance of the ICS_{Ref}, ICS_{HF} and RPR_{HF} tests with the gold standard for all women, stratifying by syphilis serological group, HIV status and malaria status. Differences between subgroups were calculated using χ^2 or Fisher's exact test as appropriate. We calculated crude and adjusted odds ratios (OR) for factors associated with syphilis serological groups (i.e.,outcome) using logistic or multinomial logistic regression analysis.

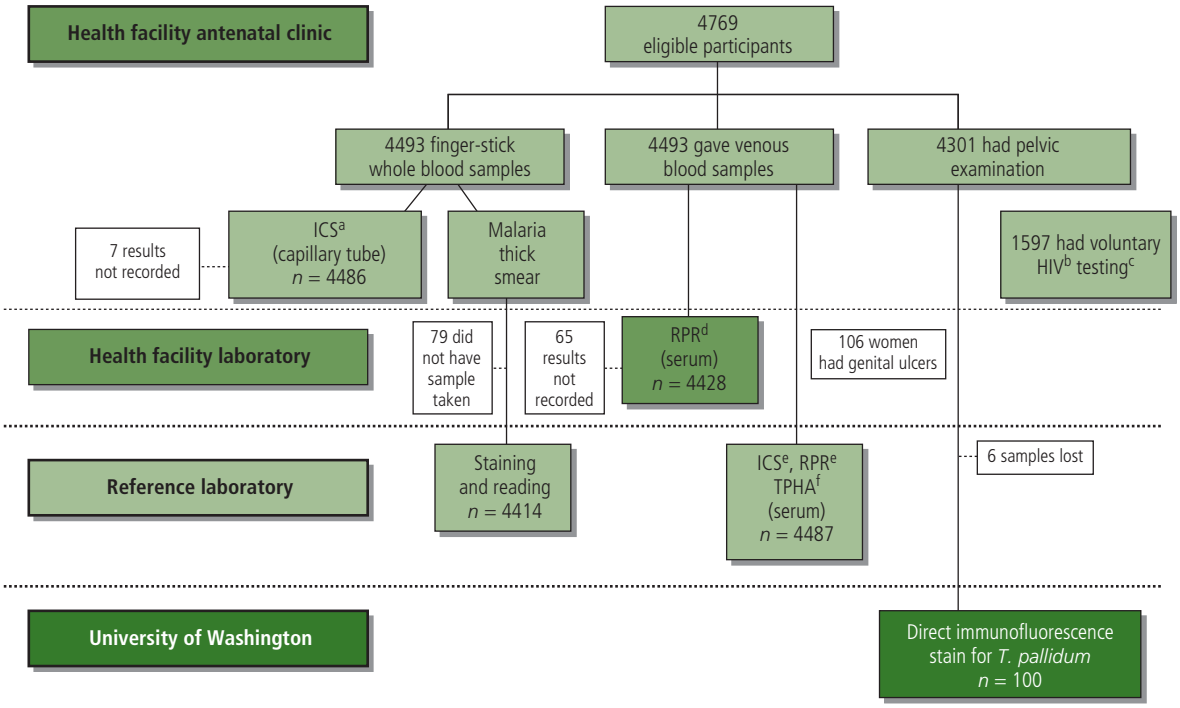
For subgroup analysis, age was treated as a categorical variable with seven groups: <15 years, 15–19, 20–24, 25–29, 30–34, 35–39, and 40 years or older. Likewise, we treated number of pregnancies as a categorical variable with six groups: 1, 2, 3, 4, 5, and 6 or more pregnancies.

The study was approved by the Instituto Nacional de Bioética para a Saúde in Mozambique and the Human Subjects Division of the University of Washington, WA, USA.

Results

Between August 2003 and January 2004, we approached 4769 women who had not had a syphilis test during their current pregnancy about participation in our study. 276 (5.8%) declined to participate. Non-systematic interviews with these women showed that the main reasons for choosing not to participate were: an unwillingness to know their HIV status (even though HIV tests were not performed as part of the study); a lack of time to go through the data collection process; and need for partner's approval. We excluded results from 6 (0.1%) women because their serum samples did

Fig. 1. **Trial flow chart**



[a] ICS = immunochromatographic strip.

[b] HIV = human immunodeficiency virus.

[c] Patients who elected voluntarily to be tested under the routine prevention of mother-to-child transmission programme gave results in our study.

[d] RPR = rapid plasma reagin.

[e] Repeated tests (blinded).

[f] TPHA = Treponema pallidum haemagglutination assay.

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not arrive at the Beira reference laboratory. Thus, data from 4487 women were included in analysis.

Seven (0.2%) ICS_{HF} test results and 65 (1.4%) RPR_{HF} test results were lost because results were not recorded after the test had been performed, but we did not exclude these participants. If the participant had a result from either ICS_{HF} or RPR_{HF} we compared that result to the gold standard.

Of the 106 samples from genital ulcers, six specimens did not arrive at the laboratory; the remaining 100 were tested with direct immunofluorescence stain for *T. pallidum*. Two samples were positive, two had inadequate volume of specimen, and 96 were negative for *T. pallidum*.

Table 1 summarizes participants' general characteristics. After controlling for health facility, we did not note any differences in socioeconomic status or syphilis prevalence between the HIV-tested women and those who did not enrol in voluntary testing. Nearly all malaria cases were asymptomatic and caused by infection with *P. falciparum*. Mean asexual parasite density was 3488 parasites/µl (±9759) in parasitaemic women.

Results of the gold standard test showed 381 (8.5%) participants with active syphilis, 150 (3.3%) old or treated cases, 46 (1.0%) biological false-positives, and 2 (0.04%) primary syphilis cases. Of the active syphilis cases, 282 (74.2%) had RPR titres ⩽ 1:8 and 29 (8%) had clinical presentations compatible with primary (n = 20) and/or secondary (n = 11) syphilis. Physical manifestations consistent with primary and secondary syphilis were poorly correlated with positive direct immunofluorescence stain for *T. pallidum*. One TPHA-positive/RPR-positive and one TPHA-negative/RPR-negative case were confirmed as primary syphilis by direct immunofluorescence stain for *T. pallidum*. Of the 318 women who reported a positive syphilis history, 212 (67%) had negative TPHA and RPR results.

Table 2 shows the agreement between TPHA (done at the Beira reference laboratory), ICS and RPR results from tests performed at the reference laboratory and the health facilities. Agreement between ICS (ICS_{HF} and ICS_{Ref}) and TPHA results and between ICS_{Ref} and ICS_{HF} results was significantly higher than for the comparison of the RPR results from different sites (P<0.001).

The coefficient of agreement between ICS_{Ref} and TPHA was significantly higher than that for the comparison of ICS_{HF} with TPHA (P = 0.002). More than two-thirds of the inter-laboratory ICS discordances were negative ICS_{HF} and positive ICS_{Ref} results.

There were 66 weak positive ICS_{Ref} results (13% of the positive ICS_{Ref} results), which accounted for 40% of the ICS_{Ref}-to-ICS_{HF} discordances. We did not note any difference in the diagnostic accuracy of the ICS with the use of EDTA or non-EDTA capillary tubes (P = 0.1). Two-thirds (n = 50) of the ICS_{Ref}-to-TPHA discordances occurred

in samples from women whose ICS_{HF}-to-ICS_{Ref} results were concordant.

Using multinomial logistic regression, we identified factors associated with discordant negative ICS_{Ref} and positive TPHA results: HIV infection (OR 3.5, (95% CI: 1.5–11)), and condylomatous lesions (4.6 [1.3–16.6]) for the all syphilis group, and malaria (3.6 (95% CI: 1.2–11.3) for the active syphilis group only. Positive ICS_{Ref} to negative TPHA results were associated with older age (1.6 (95% CI: 1.2–2.1)) and higher number of pregnancies (1.3 (95% CI: 1.1–1.5) for all syphilis cases.

Low-level reactivity RPR (titres ⩽ 1:2) were present in 100 (79.4%) of the negative RPR_{HF} to positive RPR_{Ref} discordances: we did not identify any patient variables associated with RPR_{Ref}-to-RPR_{HF} discordant results. Technicians who were unaware of previous results retested a random subsample of RPR_{Ref}-to-RPR_{HF} discordant samples, and the RPR_{Ref} result was corroborated in 41 of 45 (91%) of cases.

Table 3 shows characteristics of diagnostic accuracy of the ICS and RPR by syphilis serological group. The ICS, done both at the health facilities and the reference laboratory out-performed RPR with respect to sensitivity, specificity, and positive and negative predictive values. The differences in sensitivity between the ICS_{Ref} and ICS_{HF} tests, and between the ICS_{HF} and RPR_{HF} are statistically significant for all syphilis serologic groups shown in table 3 (P<0.001 in pair-wise comparisons).

With respect to specificity, there were significant differences between tests and sites for the all syphilis group (P<0.02). Negative predictive values were also significantly different across tests and testing sites for every syphilis serologic group (P<0.001). Positive predictive values were significantly different in the all syphilis group across tests and testing sites (P<0.006), and in active syphilis for the comparison between ICS_{Ref} and RPR_{HF} (P = 0.03). The sensitivity of the RPR_{HF} was significantly lower in 1:1 reactivity serum than in ⩾1:2 reactivity serum (51% versus 79.2%, P<0.001). We also noted significant differences between the sensitivity of the ICS_{HF} after stratification by the same serum RPR reactivity levels (77.2% vs 89.2%, P = 0.003), but not for the ICS_{Ref} (P = 0.4).

During the first month of the study, August 2003, the sensitivity of the ICS_{HF} was 90% (95% CI: 80–96). However, sensitivity decreased gradually, and by the last month had dropped to 78% (95% CI: 69–86), significantly lower than at the start of the study (χ^2 test of trends P = 0.03). This change correlated with an increase in patient numbers, higher malaria prevalence, and less frequent supervision in the clinic. We noted a similar but non-significant decline for ICS_{Ref} sensitivity.

Of the 1597 women with known HIV status, 51 (37%) of the 137 active syphilis and 20 (38%) of the 52 old or treated syphilis cases were HIV positive. Of the 4408 women with known malaria status, 53 (14%) of the 376 active syphilis and 19 (13%) of the 150 old or treated syphilis were positive for malaria. The use of different thresholds for definition of "significant" malaria parasite density did not change the test accuracy. There were too few malaria-infected women with fever (n = 8) to allow us to do subgroup analysis.

The ICS_{Ref} test was the most sensitive of the tests (P<0.01 in pair-wise comparisons), independent of malaria or HIV status. For active syphilis cases the sensitivity of the ICS_{Ref} was not significantly lower for women with HIV (P = 0.2), but sensitivity was affected by malaria coinfection (P = 0.01). However, we did not note the same pattern in participants with malaria for the ICS_{HF} results. Furthermore, the number of syphilis-positive participants who also had HIV or malaria was too small to allow us adequate power to assess differences in diagnostic accuracy in coinfected and non-coinfected groups.

The specificity of the ICS_{Ref} test in the old or treated syphilis group was higher for participants who were HIV negative (92.2%) than for HIV positive (86.4%) patients (P<0.001). The negative predictive value of the ICS_{Ref} was significantly higher in the all syphilis group for HIV negative (99.2%) than for HIV positive (97.2%) patients (P = 0.006), and in the active syphilis group for patients who did not have malaria (99.6%) compared with those who were malaria-positive (99.0%) (P = 0.01).

Table 1. **Participants' characteristics**

Characteristic	n (%)/mean ±SD[a]
Demographic characteristics	
Age (years)	23.3 ± 5.8
Estimated gestational age at first visit (weeks)	20.6 ± 6.1
Primigravidae	1323 (29.6%)
History of spontaneous abortion	496 (11.1%)
History of stillbirths	191 (4.3%)
History of any childhood death	942 (21.3%)
No electricity at home	3421 (79.2%)
No piped water at home	3503 (81.4%)
Secondary education or higher (> 6 years)	1050 (23.7%)
Self-reported medical history	
Syphilis screening (excludes primigravidae)	1708 (58.7%)
Previous syphilis diagnosis	318 (7.1%)
Previous syphilis treatment	307 (6.9%)
Prior partner syphilis history (as reported by the pregnant women)	228 (5.3%)
Don't know the partner's syphilis history	1714 (39.6%)
Other sexually transmitted infection (excludes HIV[b])	211 (4.7%)
Previous and/or current genital ulcer	219 (4.9%)
Physical examination findings	
Genital ulcer	106 (2.8%)
Condylomatous lesions	111 (2.6%)
Inguinal lymphadenopathy	1371 (31.7%)
HIV and malaria status	
HIV-infected (number and % positive; restricted to 1597 who elected to participate in voluntary testing)	387 (24.2%)
Malaria parasitemia (any level)	587 (13.3%)

[a] SD = standard deviation.
[b] HIV = human immunodeficiency virus.

There were few invalid and indeterminate TPHA results (n = 18). The proportion of such results was higher in patients with malaria (n = 6, OR 3.3 (95% CI: 1.2–8.9)). Of the 45 RPR biological false-positive cases, 8 (18%) had malaria (1.4 (95% CI: 0.7–3.1)).

Discussion

Our results show that the diagnostic accuracy of the ICS was significantly better than that of the RPR even after controlling for HIV, malaria and level of service (i.e., whether tests were done at a health facility or the reference laboratory). The accuracy of the ICS test compared favourably with that of TPHA carried out at the Beira reference laboratory, but ICS accuracy decreased when done at health facilities. That is, the accuracy of the ICS was greater when used by laboratory staff with higher levels of training and in a setting with better infrastructure and supervision than when carried out by staff at health facilities.

The sensitivity of the ICS for active syphilis in the reference laboratory decreased significantly in the presence of malaria; HIV infection did not affect the diagnostic accuracy of the ICS significantly. Even though the ICS has lower sensitivity and specificity than the TPHA, ICS could allow syphilis to be diagnosed in health facilities that do not have laboratories and the test also offers hope of improving syphilis diagnosis in facilities with laboratories.

Table 2. **Agreement and kappa coefficient of the syphilis screening tests results performed in health facilities and Beira reference laboratory**

Test/agreement	Concordance % (n)	First test[a] (-ve), second (+ve) % (n)	First test[a] (+ve), second (-ve) % (n)	Kappa
ICS_{Ref}[b] vs $TPHA_{Ref}$[c]	98.5% (4419)	1.0% (43)	0.6% (25)	0.93
ICS_{HF} vs $TPHA_{Ref}$	96.7% (4331)	2.5% (110)	0.9% (39)	0.83
ICS_{HF} vs ICS_{Ref}	97.2% (4355)	2.0% (89)	0.8% (36)	0.86
RPR_{HF}[d] vs RPR_{Ref}	94.4% (4175)	2.8% (126)	2.8% (122)	0.67

[a] First and second test refers to the order in the test/agreement column.
[b] ICS = rapid immunochromatographic strip.
[c] TPHA = *Treponema pallidum* haemagglutination assay.
[d] RPR = rapid plasma reagin.

Although the 9.5% RPR overall rate of syphilis in our sample group at first antenatal visits is high, it is lower than the 15.1% rate described for Beira in the previous 5 years from 1998–2003.[16] Reasons for this discrepancy may include a positive secular trend due to increased counselling, diagnosis and treatment especially in antenatal care or to increased condom use prompted by the AIDS epidemic. Other explanations are the incorrect performance of laboratory procedures (use of whole blood, variable time and techniques of rotation, poor conservation of reagents), low levels of supervision, and increased rates of death in the syphilis-susceptible or infected population.[32]

Self-reported syphilis history and treatment were not reliable in our study population. The proportion of women with a previous syphilis history who reported having received syphilis treatment and who had negative serologic results for all syphilis tests was higher than expected. Explanations include inaccurate recall, insufficient explanation given to patients and their partners when they receive treatment, previous false-positive RPRs, over-treatment of syphilis as a result of the use of the WHO algorithm for syndromic treatment of sexually transmitted infections, and perhaps reversion of serological tests to non-reactive after treatment.[33–35]

We compared our study results with the WHO laboratory-based evaluation of rapid syphilis diagnostics[23] using a

Table 3. **Accuracy of the ICS (immunochromatographic strip) and the RPR (rapid plasma reagin) performed in health facilities and reference laboratory (REF) by serological status**

Serological status[a]	Index test (site)	Positive index tests (n)	Sensitivity (95% CI[b])	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)
TPHA+[c] and RPR+[d,e] or RPR- (all syphilis; n = 531)	ICS_{Ref}	487	91.9% (89.2–94.1)	99.5% (99.2–99.7)	96.2% (94.2–97.7)	98.9% (98.5–99.2)
	ICS_{HF}	419	79.2% (75.5–82.6)	99.1% (98.7–99.4)	92.1% (89.2–94.4)	97.2% (96.7–97.7)
	RPR_{HF}	297	56.6% (52.2–60.9)	97.5% (96.9–97.9)	75.4% (70.8–79.6)	94.2% (93.5–94.9)
TPHA+ and RPR+ (active syphilis; n = 381)	ICS_{Ref}	366	96.3% (93.9–98.0)	96.4% (95.8–97.0)	71.3% (67.2–75.2)	99.6% (99.4–99.8)
	ICS_{HF}	326	86.0% (82.1–89.3)	96.8% (96.2–97.3)	71.0% (66.6–75.1)	98.7% (98.3–99.0)
	RPR_{HF}	272	71.9% (67.1–76.4)	96.4% (95.7–96.9)	64.9% (60.1–69.5)	97.3% (96.8–97.8)
TPHA+ and RPR- (old/ treated syphilis; n = 150)	ICS_{Ref}	121	80.7% (73.4–86.6)	91.0% (90.1–91.8)	23.6% (20.0–27.5)	99.3% (98.9–99.5)
	ICS_{HF}	93	62.0% (53.7–70.0)	91.5% (90.7–92.4)	20.3% (16.7–24.2)	98.6% (98.2–98.9)
	RPR_{HF}	25	17.0%[b] (11.3–24.0)	90.8% (89.9–91.6)	6.0% (3.9–8.7)	96.9% (96.4–97.5)

[a] One sample positive for the direct immunofluorescence stain for *T. pallidum* was negative for all serological tests.
[b] CI = confidence interval.
[c] TPHA = *Treponema pallidum* haemagglutination assay.
[d] RPR+ results in this category represent false-positive results at the health facility and according to the definition, sensitivity should be 0.
[e] RPR = rapid plasma reagin.

random subsample of 400 sera, and we found no significant differences with the sensitivity (χ^2 test $P = 0.09$) and specificity ($P = 0.5$) of our ICS_{Ref}. Compared with other field studies, our data on the sensitivity of the RPR_{HF} for active syphilis showed no significant differences to those reported in the Gambia ($P>0.3$)[36] and in Senegal ($P>0.5$),[37] but our sensitivity was lower than that reported in a South African study ($P<0.01$).[38]

Antenatal screening for syphilis is usually done with non-treponemal tests, either alone or in combination with treponemal tests.[6, 9, 25, 27, 28, 30, 38] However, the use of a treponemal test as the only means to diagnose syphilis has important public health implications. About 20% of pregnant women who had a positive result from the ICS_{HF} test were TPHA-positive/RPR-negative (2.1% of all women tested). However, only 14% of the TPHA-positive/RPR-negative women reported previous syphilis treatment.

In Mozambique there are about one million first antenatal visits every year. Using the ICS_{HF} as the principal screening test, we would correctly detect 93 800 cases of syphilis every year, assuming the same syphilis prevalence and ICS_{HF} recorded in our study. From this group of 93 800 women, about 27 000 (15 000 TPHA-positive/RPR-negative and 12 000 TPHA-positive/RPR-positive cases) would not be diagnosed with use of the RPR_{HF} test. The difference could exceed 20 600 for each of these serological groups if the quality of testing at the health facilities were equal to that of the reference laboratory.

Although with the ICS we would detect more active syphilis cases than are currently detected with RPR, we would also detect more TPHA-positive/RPR-negative cases. Whether these patients are truly past treated cases of syphilis or patients with late untreated syphilis, active syphilis with false-negative RPR, or very early primary syphilis is difficult to know.[25] Women with untreated syphilis, particularly if co-infected with HIV, are at risk of having syphilis complications (i.e. neurosyphilis and other tertiary manifestations)[34, 39, 40] and may pass on the infection to their child or to their sexual partners. In settings of high HIV seroprevalence and poor availability of syphilis diagnosis and treatment, patients who are TPHA-positive/RPR-negative would probably benefit from treatment.

Women who have had a previous syphilis diagnosis and treatment and who are screened with the ICS test in subsequent pregnancies will probably again test positive for the disease. As a result, they and their sexual partners will most likely be offered treatment during each pregnancy. Since syphilis is a sexually-transmitted disease, repeated notification and treatment of sexual partners may place women at risk of domestic violence and family break-ups.

Although this concern about having positive syphilis tests repeatedly in subsequent pregnancies (after receiving appropriate treatment in a previous pregnancy) is more important in relation to the use of treponemal tests, it is not limited to those tests. Especially if time between subsequent pregnancies is short (i.e., there is no time for the non-treponemal test to become negative), and there are neither follow-up quantitative RPRs, nor clinical records.

In view of the small sample sizes in our study, our findings about differences of diagnostic accuracy between patients with malaria or HIV, or both should be interpreted with caution. However, if true, the described differences may have important clinical implications in areas with high rates of HIV and malaria.

The ICS test is easy to perform. However, the lowered diagnostic accuracy at health facilities compared with the reference laboratory, and the decrease in accuracy during the course of the study is cause for concern. To obtain consistently accurate results, ongoing training and systematic supervision with regular quality control are necessary. Particular emphasis should be made on recognizing weak-positive ICS results. A good light source is essential for more accurate ICS test results. We did not systematically measure laboratory temperature, so can not describe the association between test performance and ambient temperature.

Widespread use of the ICS in Mozambique and comparable settings would result in a substantial improvement in local capacity to prevent congenital syphilis. Furthermore, use of ICS would allow timely detection and treatment of the disease, thus reducing maternal, perinatal and infant mortality and morbidity in the region.

Our findings are important for the calculation of the cost-effectiveness of the intervention. They also show the need to ascertain the rate of reversion to ICS-negative in syphilis-infected patients who have had appropriate treatment. Furthermore, it will be important to define more clearly the effects of immune-function modifiers on the diagnostic accuracy of the test. Finally, it is critical to design interventions that will promote high levels of accuracy in testing that are sustainable in health facility settings. ■

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Résumé

Comparaison de la précision diagnostique d'un test immunochromatographique rapide et du test rapide à la réagine pour le dépistage prénatal de la syphilis au Mozambique

Objectif Les programmes de lutte contre la syphilis dans les pays en développement se heurtent à l'insuffisance des services de type analytique, aux retards de diagnostic et aux doutes que suscitent les méthodes actuelles de dépistage. L'étude visait à comparer la précision diagnostique d'un test immunochromatographique rapide en bandelette (ICS) et du test rapide à la réagine (RPR) avec la méthode combinée de référence (RPR, test d'hémagglutination du tréponème pâle combiné au test d'immunofluorescence directe dans un laboratoire de référence) pour le dépistage de la syphilis au cours de la grossesse.

Méthodes L'étude a pris en compte les résultats des tests de 4789 femmes ayant subi leur première visite prénatale dans l'un des six centres de santé de la Province de Sofala au centre du Mozambique. Elle a comparé la précision diagnostique (sensibilité, spécificité et valeurs prédictives positives et négatives) des tests de type ICS et RPR pratiqués dans les centres de santé et de l'ICS effectué au laboratoire de référence. Des comparaisons ont également été réalisées dans des sous-groupes définis en fonction du statut à l'égard du VIH et du paludisme.

Résultats Pour la syphilis active, la sensibilité du test ICS était de 95,3 % au laboratoire de référence et de 84,1 % dans le cadre d'un centre de santé. La sensibilité du test RPR pratiqué dans un centre de santé était de 70,7 %. Pour la spécificité et les valeurs prédictives positives et négatives, on a observé des différences analogues. L'ICS a donné de meilleurs résultats que le RPR dans toutes les comparaisons ($p<0,001$).

Conclusion La précision diagnostique de l'ICS n'est pas très éloignée de celle de la méthode de référence. L'utilisation de ce test au Mozambique et dans des contextes similaires pourrait améliorer le diagnostic de la syphilis dans les centres de santé, qu'ils soient dotés ou non d'un laboratoire.

Resumen

Comparación de la precisión diagnóstica de una prueba inmunocromatográfica rápida y de la prueba de reagina rápida en plasma para el cribado de la sífilis prenatal en Mozambique

Objetivo En los países en desarrollo los programas de control de la sífilis tropiezan con la falta de servicios de laboratorio, las demoras del diagnóstico y las dudas existentes respecto a los actuales métodos de cribado. Decidimos comparar la precisión diagnóstica de una prueba con tira inmunocromatográfica (IC) y de la prueba de reagina rápida en plasma (RRP) con la prueba de referencia combinada (RRP, hemaglutinación de *Treponema pallidum* e inmunofluorescencia directa en un laboratorio de referencia) para la detección de la sífilis en el embarazo.

Métodos Consideramos los resultados analíticos correspondientes a 4789 mujeres que realizaron su primera visita prenatal en alguno de los seis centros de salud elegidos en la provincia de Sofala (Mozambique central). Comparamos la precisión diagnóstica (sensibilidad, especificidad, y valores predictivos positivo y negativo) de la IC y la RRP realizadas en los centros de salud y la IC realizada en el laboratorio de referencia. Hicimos también comparaciones de subgrupos en función del estado serológico respecto al VIH y la malaria.

Resultados Para la sífilis activa, la sensibilidad de la IC fue de un 95,3% en el laboratorio de referencia, y de un 84,1% en el centros de salud. La sensibilidad de la RRP en este último fue del 70,7%. La especificidad y los valores predictivos positivo y negativo mostraron diferencias similares. La IC superó a la RRP en todas las comparaciones ($P < 0,001$).

Conclusión La precisión diagnóstica de la IC fue buena en comparación con la prueba de referencia. En Mozambique y en otros entornos semejantes, la IC permitiría mejorar el diagnóstico de la sífilis en los centros de salud, tengan o no laboratorio.

ملخص

مـــقارنة بين الدقة التشخيصية لاختبار الاستشراب المناعي السريع ولاختبار الراجنة البلازمية السريع المستخدمَيْن لتحرِّي الزهري قبل الولادة في موزامبيق

الهدف: تتعرَّض برامج مكافحة الزهري في البلدان النامية لعراقيل بسبب نقص الخدمات المختبرية، وبطء التشخيص، وعدم الثقة في طرق التشخيص الحالية. وقد استهدفت هذه الدراسة المقارنة بين الدقة التشخيصية لاختبار الاستشراب المناعي والدقة التشخيصية لاختبار الراجنة البلازمية السريع، باستخدام المعيار الذهبي المشترك (الراجنة البلازمية السريعة، ومقايسة التراص الدموي للّولبية الشاحبة، والتألق المناعي المباشر الذي يُجرى في مختبر مرجعي)، وذلك لاكتشاف الزهري لدى الحوامل.

الطريقة: تم تحليل نتائج اختبار 4789 امرأة ممن يحضرن أول زيارة لتلقِّي الرعاية قبل الولادة في واحد من المرافق الصحية الستة في منطقة سوفالا، في وسط موزامبيق. وقمنا بالمقارنة بين دقة التشخيص (من حيث الحساسية، والنوعية، والقيم التنبؤية الموجبة والسالبة) لكل من اختبار الاستشراب المناعي واختبار الراجنة البلازمية السريع، اللذين أُجريا في المرافق الصحية، وبين اختبار الاستشراب المناعي الذي أُجري في المختبر المرجعي. كما أجرينا مقارنات بين المجموعات الفرعية وفقاً للوضع المتعلق بفيروس الإيدز والملاريا.

الموجودات: بالنسبة للزهري النشط، بلغت حساسية اختبار الاستشراب المناعي 95.3% في المختبر المرجعي، في حين بلغت حساسيته 84.1% في المرفق الصحي. وكانت حساسية اختبار الراجنة البلازمية السريع الذي أُجري في المرفق الصحي 70.7%. وأظهرت النوعية والقيم التنبؤية الموجبة والسالبة نمطاً متماثلاً. وقد امتاز اختبار الاستشراب المناعي على اختبار الراجنة البلازمية السريع في جميع المقارنات (قيمة الاحتمال أقل من 0.001).

الاستنتاج: إن الدقة التشخيصية لاختبار الاستشراب المناعي تتوافق مع دقة المعيار الذهبي. ومن الممكن أن يؤدي استخدام اختبار الاستشراب المناعي في موزامبيق والأماكن المماثلة الأخرى إلى تحسين دقة تشخيص الزهري في المرافق الصحية المزودة بمختبرات أو غير المزودة بها.

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