Performance of the rapid plasma reagin and the rapid syphilis screening tests in the diagnosis of syphilis in field conditions in rural Africa

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ORIGINAL ARTICLE

Objective: To assess the rapid plasma reagin (RPR) test performance in the field and to evaluate a new rapid syphilis test (RST) as a primary screen for syphilis.

Methods: 1325 women of reproductive age from rural communities in the Gambia were tested for syphilis seropositivity using a RPR 18 mm circle card and a RST strip. Within 1 week a repeat RPR and a TPHA test were carried out using standard techniques in the laboratory.

Results: Comparing field tests to a diagnosis of “active” syphilis defined as laboratory RPR and TPHA positive, the RPR test was 77.5% sensitive and 94.1% specific; the RST was 75.0% sensitive and 95.2% specific. The RST was easier to use and interpret than the RPR test especially where field conditions were difficult. In this setting with a low prevalence of syphilis in the community (3%), the chance of someone with a positive test being confirmed as having serologically active syphilis was less than 50% for both tests.

Conclusions: The appropriateness of syphilis screening using RPR testing in antenatal clinics and health centres should be questioned if there is a low prevalence in the population, conditions for testing are poor, and resources limited. There is still an urgent need for an appropriate rapid syphilis test for field use.

The rapid plasma reagin (RPR) 18 mm circle card test for syphilis is used as a screening test in many antenatal clinics and health facilities in the developing world. Although it is easy to perform and inexpensive it may be difficult to interpret and requires training of health personnel to ensure testing is carried out and results are read correctly. The test specificity can be limited owing to the non-specific nature of the cardiolipin antigen as biological false positives occur; these can be due to viral infections, malaria, and pregnancy. Additionally, false negatives may occur both in early primary cases and in patients with secondary syphilis, as a result of prozone reactions; this may limit the sensitivity of the test. In many developing country settings where the RPR test would be useful as a screening test, such as antenatal clinics, quality control procedures are suboptimal or lacking entirely and the rate of false positives and false negatives associated with the use of the test (and consequent overtreatment or undertreatment for syphilis) may be higher under operational conditions than that anticipated from research reports. We assessed the RPR test performed under field conditions against RPR/TPHA testing performed in a well appointed laboratory. Testing was carried out in the Gambia, where the national prevalence of serologically active syphilis was recorded as 2.8% in a survey in 1995 (O’Donovan et al, unpublished data) but has been reported as high as 7% in 15–34 year old women in some districts. We also evaluated the performance of a rapid syphilis test (RST, Quorum Diagnostics, Vancouver, BC, Canada) as a primary screen. The RST is a one step immunochromatographic strip test, utilising a 47 kDa recombinant antigen of Treponema pallidum to detect antibody, developed by Omega Diagnostics in association with the Programme for Appropriate Technology in Health (PATH) and UNAIDS, Sexually Transmitted Diseases Initiative.

MATERIALS AND METHODS
A total of 1325 women aged 15–54 participated in a large community based reproductive health survey in 20 villages in the Farafenni area of the Gambia, which is described elsewhere. Syphilis testing was included as part of the survey. For this testing a field laboratory was set up in each village. All necessary equipment and consumables were transported daily to the site being surveyed. A portable generator provided electricity for the centrifuge and shaker. All reagents, RPR kits, rapid syphilis test strips, and samples collected were kept in a cool box that was replenished with ice packs daily.

For RPR testing a 10 ml venous blood sample was collected into a plain vacutainer, allowed to clot for about 15 minutes, and centrifuged for 10 minutes at 2000 g. A standard RPR 18 mm circle card test (Quorum Diagnostics) was carried out, mixing one drop of serum with one drop of RPR reagent, mixing on a shaker for 8 minutes, and read in the best available light. Positive and negative control sera were included in each day’s testing.

For RST testing, 100 µl of serum was aliquoted into a fresh serum tube. A RST strip was removed from the foil pouch and added to the tube. This was left for 15 minutes and the results read, according to the manufacturer’s guidelines. Where the sera reacts with the Treponema pallidum recombinant antigens in the strip a double pink line results and these were read as positive. Sera were regarded as negative if only the single control line was visible. If no pink line occurred the test was discarded as invalid.

At the end of each day samples were returned to the well equipped laboratory at the MRC Laboratories field station at Farafenni, which has a constant power and water supply. Samples were received, catalogued, and stored frozen. Within 1 week RPR and TPHA testing was carried out using standard techniques. The same laboratory assistant performed the tests in the laboratory as in the field but did not have access to field results.

The TPHA was a standard Fujeriebo test (Mast Laboratories, UK). Sera were diluted to 1/160 and mixed with sensitised and unsensitised red blood cells. This was read after 1 hour at room temperature. Sera were considered positive if agglutination
occurred with sensitised cells only. Samples were considered void if agglutination occurred with unsensitised cells.

RESULTS

From the 1325 serum samples obtained, 1295 samples were RPR tested in the field, and all 1325 samples were tested in the laboratory; the 30 women not screened in the field were revisited and offered treatment if positive results were subsequently found. Field screening in these 30 women was not carried out owing to logistical difficulties, either generator or equipment failure or lack of consumables in the field laboratory. In the field 76 samples were read as RPR positive (5.9%). In the laboratory, 47 samples were read as RPR positive (3.5%), 16 as weakly positive (1.2%), and 40 (3.1%) were RPR/TPHA positive. Using the rapid syphilis strips 92 samples were positive; of these 33 were RPR positive, 51 TPHA positive, and 30 positive by both tests in the laboratory.

The performance of the field RPR and RST tests against serologically active syphilis (defined by laboratory RPR positive and TPHA positive) is shown in table 1. Calculations of sensitivity and specificity against this standard and of positive and negative predictive values for this population (where the prevalence of active syphilis is about 3%) are also presented.

Table 1 Comparison of RPR testing in the field and the laboratory and the rapid syphilis test in defining cases of “active” syphilis

<table>
<thead>
<tr>
<th>Field RPR test</th>
<th>Yes</th>
<th>No</th>
<th>Total</th>
<th>Test performance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>31</td>
<td>45</td>
<td>76</td>
<td>Sensitivity 77.5%</td>
</tr>
<tr>
<td>Negative</td>
<td>9</td>
<td>1210</td>
<td>1219</td>
<td>Specificity 96.4%</td>
</tr>
<tr>
<td>Total</td>
<td>40</td>
<td>1255</td>
<td>1295</td>
<td>PPV/NPV 40.8/99.3%</td>
</tr>
<tr>
<td>Rapid syphilis test</td>
<td>Yes</td>
<td>No</td>
<td>Total</td>
<td>Test performance</td>
</tr>
<tr>
<td>Positive</td>
<td>30</td>
<td>62</td>
<td>92</td>
<td>Sensitivity 75.0%</td>
</tr>
<tr>
<td>Negative</td>
<td>10</td>
<td>1223</td>
<td>1233</td>
<td>Specificity 95.2%</td>
</tr>
<tr>
<td>Total</td>
<td>40</td>
<td>1285</td>
<td>1325</td>
<td>PPV/NPV 32.6/99.2%</td>
</tr>
</tbody>
</table>

Table 2 Comparison of RPR testing in the field and the laboratory

<table>
<thead>
<tr>
<th>Field RPR test</th>
<th>Laboratory RPR test</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>35</td>
<td>1</td>
<td>41</td>
<td>76</td>
</tr>
<tr>
<td>Negative</td>
<td>12</td>
<td>1207</td>
<td>1219</td>
<td>1231</td>
</tr>
<tr>
<td>Total</td>
<td>47</td>
<td>1248</td>
<td>1295</td>
<td>1325</td>
</tr>
</tbody>
</table>

Table 3 Comparison of rapid syphilis test and TPHA results

<table>
<thead>
<tr>
<th>Field RPR test</th>
<th>Laboratory TPHA test</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>51</td>
<td>41</td>
<td>92</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>29</td>
<td>1204</td>
<td>1233</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>80</td>
<td>1245</td>
<td>1325</td>
<td></td>
</tr>
</tbody>
</table>

discussion

The last guidelines for serological diagnosis for syphilis, produced by the World Health Organization, recommended the use of a cardiolipin test such as the RPR and the TPHA for screening purposes. These guidelines are still in place in many countries but with the development of sensitive and specific treponemal antigen based enzyme immunoassays (EIA) they have been extended in some countries, including the United Kingdom. Results using these assays now suggest a sensitive EIA, as a single screening test would give similar results to RPR and TPHA in combination. In areas where ELISA technology is readily available screening can be automated and more standard reliable results obtained. In addition, the FTA-abs, previously considered as the “gold standard” confirmatory test, has been shown to have a poor specificity and is being superseded by newer, easier antitreponemal IgM ELISAs. In this study we use the traditional standard of laboratory RPR and TPHA positive to indicate active syphilis and we compared this standard both with RPR carried out in field conditions that are typical of many developing country health centres and with the newly developed RST strip. There is little information available on the performance of syphilis tests under field conditions, although decentralised syphilis prevention programmes in antenatal clinics using RPR testing has been recommended. A study in an antenatal clinic in South Africa using RPR testing showed that clinic testing had a sensitivity of 92.8% and a specificity of 96.3% when compared to reference laboratory results, which led to its recommendation for use. In contrast, Van Dyck et al using the RPR teardrop test in field clinics found it to be 69.7% sensitive and 96.5% specific compared to standard RPR/TPHA tests and concluded it was not reliable in these circumstances. The intermediate sensitivity of 77.5% we found here for field RPR testing is closer to that found in the latter study.

The new RST was easier to use and easier to interpret than the RPR test especially where field conditions were difficult. The RPR test especially where field conditions were difficult.
Table 4 The calculated predictive values of the field RPR and RST at different active syphilis prevalences

<table>
<thead>
<tr>
<th>Prevalence of active syphilis</th>
<th>Test:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probability of syphilis when test is positive</td>
<td>RST</td>
</tr>
<tr>
<td>2%</td>
<td>3%</td>
</tr>
<tr>
<td>Field RPR</td>
<td>24.2%</td>
</tr>
<tr>
<td>Field RPR</td>
<td>30.5%</td>
</tr>
<tr>
<td>Probability of syphilis when test is negative</td>
<td>RST</td>
</tr>
<tr>
<td>0.53%</td>
<td>0.80%</td>
</tr>
<tr>
<td>Field RPR</td>
<td>0.47%</td>
</tr>
</tbody>
</table>

Key messages

- The RPR test does not perform well in hot, dusty field conditions such as are found in many developing country health centres.
- The rapid syphilis screening test has the same sensitivity and specificity as RPR but measures specific treponema antibodies.
- Use of screening depends upon prevalence in a population to make it worthwhile.

Acknowledgements

This work was supported by the Medical Research Council; RPR, TPHA, and rapid syphilis tests were supplied by Quorum Diagnostics Ltd, Vancouver, BC, Canada.

Contributors

BW designed the study, coordinated the laboratory testing, and drafted the report; GW conceived and designed a larger study on reproductive health of which this study was a part, coordinated the fieldwork, and edited the report; LM contributed to the study design, was responsible for handling and analysis of data, and edited the report; RB contributed to fieldwork and analysis of data; RB contributed to study design, analysis of data, and edited the report.
REFERENCES


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