Strategies of testing for syphilis during pregnancy

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RHL Summary

Key findings

In comparing conventional syphilis testing to on-site non-treponemal testing, and on-site syphilis testing (including on-site rapid treponemal testing at the first antenatal visit with first dose of treatment and partner treatment provided if positive results, and counseling and third trimester second screening provided if negative results), this review found:

- A significant reduction in the incidence of congenital syphilis and improvement in the proportion of pregnant women being tested for syphilis in the on-site testing group;
- Syphilis detection rates, adequate treatment rates (defined as the percentage of sero-positive cases completing three doses of benzathine penicillin before delivery), and partner treatment (treatment of sexual partners of seropositive women) were improved in the point-of-care testing group;
- No benefits in reduction of perinatal mortality were seen in the only trial reporting on this outcome. However, no adjustment for cluster design was done for this outcome;
- No data on incidence of HIV/AIDS, obstacles in uptake of screening, adverse events and other pre-specified outcomes; and
- Measures of effectiveness were not comparable and thus were presented separately.

Evidence included in this review

Two cluster-randomized trials were included, involving 8493 women. One trial was conducted in Mongolia and randomized 14 clinics to conventional syphilis testing versus one-stop service. The second trial was conducted in South Africa and compared on-site syphilis non-treponemal testing and treatment strategy during antenatal control to traditional laboratory testing.

Quality assessment

Studies were judged to be at high or unclear risk of bias.

Clinical implications

Offering pregnant women on-site rapid treponemal syphilis screening tests seems to have an impact on syphilis detection, early and adequate treatment and reductions in congenital syphilis when compared to conventional syphilis infection tests. Treatment delay was significantly decreased in the trial using non-treponemal on-site screening method. Other factors such as setting characteristics as well as technical, logistical and staffing obstacles, may influence results.
Further research

Future trials should assess relevant maternal and perinatal outcomes as well as implementation difficulties for different testing strategies at individual and health system levels while minimizing risk of bias.

Cochrane review


Abstract

Each year about two million pregnant women are infected with preventable syphilis infection, mostly in developing countries. Despite the expansion of antenatal syphilis screening programmes over the past few decades, syphilis continues to be a major public health concern in developing countries. Point-of-care syphilis testing may be a useful strategy to substantially prevent syphilis-associated perinatal mortality and other negative consequences in resource-poor settings. However, the evidence on effectiveness has been generated mostly from observational study designs or has been reported as a mixed-intervention effect.

To assess the effectiveness of antenatal syphilis screening in improving the uptake of screening tests and treatment, and reducing perinatal mortality.

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (30 September 2014) and the reference lists of retrieved studies.

Randomised (individual and cluster) controlled trials comparing different screening tests conducted during routine antenatal check-ups versus no screening test. Cross-over trials and quasi-randomised experimental study designs were not eligible for inclusion.

Two review authors independently assessed trials for inclusion and risk of bias, extracted data and checked for accuracy.

We included two cluster-randomised controlled trials (three reports). Both trials assessed point-of-care syphilis testing with conventional testing methods and together involved a total of 8493 pregnant women. Data from these trials were not amenable to meta-analysis as the measure of effectiveness was assessed in a non-comparable way.

One trial randomised 14 antenatal clinics (including 7700 pregnant women) and was carried out at in Ulaanbaatar, Mongolia. The trial assessed one-stop syphilis testing using a rapid treponemal test, and was judged to have unclear methods of random sequence generation, allocation concealment, selective reporting, and other bias and low risk of bias for incomplete outcome data. Blinding was not reported and was assessed as high risk. The point-of-care testing provided screening, test results and treatment within the same day. The trial appears to have adjusted their results to account for clustering. We entered the data into RevMan using the generic inverse variance method. The incidence of congenital syphilis was lower in the clusters receiving on-site screening (adjusted odds ratio (AOR) 0.09, 95% confidence interval (CI) 0.01 to 0.71) and the proportion of women tested for syphilis was higher in the clusters receiving on-site screening at both the first antenatal visit and at the third trimester visit (OR 989.80, 95% CI 16.27 to 60233.05; OR 617.88, 95% CI 13.44 to 28399.01). Adequate treatment and partner treatment was higher with the on-site screening (AOR 10.44, 95% CI 1.00 to 108.99; AOR 18.17, 95% CI 3.23 to 101.20) and more syphilis cases were
detected at first and third trimester visits with the on-site screening (AOR 2.45, 95% CI 1.44 to 4.18; AOR 6.27, 95% CI 1.47 to 26.69). Perinatal mortality, incidence of HIV/AIDS, obstacles in uptake of screening, any other adverse effects, or healthcare resource usage were not reported in this trial.

The second trial divided clinics into seven matched pairs (including 7618 pregnant women, although results were only presented for the positive cases (793 women)), and within each pair one clinic was randomised to receive the on-site screening and the other to continue routine laboratory testing. The trial was conducted in primary healthcare clinics in KwaZulu-Natal, South Africa. Random sequence generation were judged to be at low risk of bias, but allocation concealment and incomplete outcome data were judged to be high risk. Other bias and selective reporting bias remain unclear. Blinding was not reported and was assessed as high risk of bias. This trial assessed the primary outcome of this review (perinatal mortality) and the secondary outcomes (adverse outcomes; adequate treatment; syphilis prevalence) in the subset of women (793 women) who tested positive for syphilis. Only one outcome, adequate treatment, was adjusted to account for cluster design. However, not enough information was provided to include this in an analysis using the generic inverse variance method. Where possible, results have therefore been presented in forest plots (perinatal mortality; adequate treatment), as if the data are from a parallel randomised controlled trial. These results should therefore be interpreted with caution.

The trial reported on perinatal mortality in women with positive test results and showed that on-site screening using a rapid plasma reagin test had no clear evidence of an effect on perinatal mortality reduction (odds ratio (OR) 0.63; 95% CI 0.27 to 1.48; 18/549 (3.3%) versus 8/157 (5.1%)). After loss to follow up, 396/618 (64.1%) women with positive test results received adequate treatment (two or more doses of 2.4 mega units of benzathine penicillin) in the intervention cluster versus 120/175 (68.6%) in the control (OR 0.82; 95% CI 0.57 to 1.17). It was not possible to include any other data on reported outcomes in forest plots (adverse outcomes; syphilis prevalence). Incidence of congenital syphilis, proportion of women test for syphilis, incidence of HIV/AIDS, obstacles in uptake of screening, partner treatment, or healthcare resource usage were not reported in this trial.

This review included evidence from two cluster-randomised trials at high or unclear risk of bias for most of the 'Risk of bias' domains. Data were not combined in meta-analysis because the trials used non-comparable measures of effectiveness.

Point-of-care syphilis testing showed some promising results for syphilis detection and treatment rates and for use in different settings. In Mongolia point-of-care testing was found to be effective in increasing the proportion of pregnant women tested for syphilis and treatment provided, reducing congenital syphilis, and improving access to treatment for both women and their partners. In contrast, in rural South Africa, among women with positive test results, there was no clear evidence of an effect of point-of-care syphilis testing in increasing adequate syphilis treatment rates, and reducing perinatal mortality, but point-of-care testing was found to reduce delay in seeking treatment.

More trials are therefore warranted to determine the effectiveness of available testing strategies for improving syphilis-associated adverse outcomes in pregnant women and neonates, especially in high-risk regions.


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