Effect of a syphilis control programme on pregnancy outcome in Nairobi, Kenya

M Temmerman, P Gichangi, K Fonck, L Apers, P Claeyts, L Van Renterghem, D Kiragu, G Karanja, J Ndinya-Achola, J Bwayo

Objectives: To assess the impact of a syphilis control programme of pregnant women on pregnancy outcome in Kenya.

Method: Women who came to deliver to Pumwani Maternity Hospital (PMH) between April 1997 and March 1998 were tested for syphilis. Reactive rapid plasma reagin (RPR) tests were titrated and confirmed with treponema haemagglutination test (TPHA). Equal numbers of RPR and TPHA negative women were enrolled. Antenatal syphilis screening and treatment history were examined from the antenatal cards.

Results: Of 22 466 women giving birth, 12 414 (55%) were tested for syphilis. Out of these, 377 (3%) were RPR reactive of whom 296 were confirmed by TPHA. Syphilis seroreactive women had a more risky sexual behaviour and coexistent HIV antibody positivity; 26% were HIV seropositive compared with 11% among syphilis negative mothers. The incidence of adverse obstetric outcome defined as low birth weight and stillbirth, was 9.5%. Syphilis seropositive women had a higher risk for adverse obstetric outcome (OR 4.1, 95% CI 2.4–7.2). Antenatal treatment of RPR reactive women significantly improved pregnancy outcome but the risk of adverse outcome remained 2.5-fold higher than the risk observed in uninfected mothers.

Conclusions: These data confirm the adverse effect of syphilis on pregnancy outcome. This study also shows the efficacy of antenatal testing and prompt treatment of RPR reactive mothers on pregnancy outcome.

Introduction

Despite being easily detectable and treatable in pregnancy, syphilis remains an important cause of adverse pregnancy outcome. The prevalence of reactive syphilis serology among pregnant women in Africa ranges from 6% to 16%. At a level of seroreactivity of 10%, 5–8% of pregnancies will result in adverse outcome due to syphilis, such as spontaneous abortion, perinatal or infant death, or an infant with congenital syphilis. Screening and treatment of syphilis during pregnancy is considered to be highly cost effective. In theory, syphilis control in pregnancy is a national health policy in many countries, but in reality this intervention is often not implemented in poor resource countries with high syphilis prevalence because of financial, operational, and logistical constraints.

In Kenya, a national congenital syphilis control programme has been in place for more than 20 years. In Nairobi, the programme is organised by the public health outcome of the Nairobi City Council (NCC) and has been subject to monitoring, evaluation, and innovation since the early 1990s. Initially, all women attending antenatal clinics were bled at the clinic and the blood samples were transported to a central laboratory. Rapid plasma reagin (RPR) reactive patients were referred for treatment to a central STD clinic. In 1992, a cost effectiveness analysis of the syphilis control strategy revealed that less than 60% of new antenatal attendees in the city council clinics were screened and only 9% of RPR positive women were adequately treated. This led to an intervention supported by the Commission of the European Communities (CEC) whereby the formerly centralised syphilis screening programme was decentralised to 10 large antenatal clinics governed by the Nairobi City Council.

These 10 intervention clinics were strengthened to perform RPR card testing and provide treatment on the spot at the time of the first antenatal visit. As a result of this new approach virtually all pregnant women attending one of these intervention clinics were screened, and 87% of seroreactive women were treated on site as well as 50% of their partners.

Five years after the initiation of this decentralised approach in Nairobi, it was considered appropriate to re-evaluate the whole programme. The major objectives of the assessment were to measure (1) risk factors for syphilis at delivery, (2) the effect of syphilis on pregnancy outcome, and (3) the impact of the decentralised programme of screening and prompt treatment on pregnancy outcome.

Materials and methods

The study was conducted from April 1997 to March 1998 at Pumwani Maternity Hospital, Nairobi, Kenya. The Pumwani Maternity Hospital serves as the major referral maternity hospital for the city and its environs. The hospital caters mainly for women from lower socioeconomic classes. An average of 60 deliveries takes place every day.

Women were invited to participate in the study within 24 hours after delivery. For logis-
tic reasons enrolment took place during working hours only, but all women who had given birth in the previous 24 hours were eligible. After obtaining informed consent, a structured questionnaire including sociodemographic, medical, and obstetric data was administered, and pre-HIV test counselling and medical examination were performed. Blood samples for syphilis and HIV tests were taken. All RPR positive mothers were treated with a single dose of benzathine penicillin G 2.4 MU intramuscularly. All women were invited to the follow up clinic 7–14 days post partum. HIV post-test counselling was done during this visit and subsequent postnatal visits. Following the national guidelines, HIV infected women were advised to breast feed, unless they had access to safe and affordable alternatives. This population of poor women, however, had no choice but to continue breast feeding. For every RPR and TPHA positive woman, the next RPR and TPHA negative woman was enrolled.

Antenatal cards of all women delivering in Pumwani Maternity Hospital during the study period were examined. The antenatal clinic where the RPR test was done, the result of the test, as well as the treatment status were recorded. From the antenatal card it was clear whether the patient attended an intervention or non-intervention clinic.

Ethical clearance for the study was obtained from the Kenyatta National Hospital ethics and review committee.

CASE DEFINITIONS

Adverse obstetric outcome was defined as a baby with low birth weight (less than 2500 g) or a stillborn (a dead fetus after 20 weeks or with a birth weight over 500 g).

Maternal syphilis classification: (1) active syphilis when RPR was reactive and TPHA was positive; (2) old syphilis infection when RPR was negative and TPHA positive; (3) false positive RPR test or early infection in case of a positive RPR test and negative TPHA; (4) patients who were both RPR and TPHA negative were categorised as not infected.

Women who were found to be RPR negative and TPHA positive at delivery after initial syphilis treatment during this index pregnancy were considered cured.

For assessing risk factors of syphilis and the impact on pregnancy outcome (objective 1 and 2), only syphilis results at delivery were taken into account. For the estimation of the effect of treatment on pregnancy outcome (objective 3), four subgroups were considered: (1) syphilis seronegative in pregnancy and at delivery; (2) RPR reactive during pregnancy, treated, and syphilis seronegative at delivery; (3) RPR reactive during pregnancy, treated and still syphilis seropositive at delivery; (4) syphilis seropositive during pregnancy and delivery and not treated, or RPR negative during pregnancy and RPR seroreactive at delivery (table 1).

LABORATORY PROCEDURES

Serum samples were analysed at the department of medical microbiology, University of Nairobi, and quality control was done by the University of Ghent. Syphilis serology was performed using the rapid plasma reagin card test (RPR, Becton Dickson, MD, USA) and positive samples were titrated. Confirmation tests were done with the Treponema pallidum haemagglutination test (TPHA, Randox Laboratories, UK). HIV screening was done using the enzyme linked immunosassay (Biochem Immuno Systems Kit, Montreal, Canada) and positive samples were confirmed using double ELISA (Biotech Ltd, Cambridge, Ireland).

STATISTICAL METHODS

Data analysis was done using SPSS version 7.5. The $\chi^2$ test with Yates’s correction was used to compare proportions and the $t$ test to compare sample means. Odds ratios (OR) and their 95% confidence intervals (CI) were used to measure strength of associations.

Results

From April 1997 to March 1998, a total of 22 466 women delivered in Pumwani Maternity Hospital; 12 414 (55%) women were screened for syphilis at delivery. Of those, 35% had attended one of the intervention clinics while 55% had received antenatal care in any of the other clinics, and 10% were unbooked.

The incidence of low birth weight was 8.8% while 1.8% of the infants were stillborn. The incidence of multiple gestation was 1.8%. The mothers of these babies were excluded from the study because of anticipated practical problems at follow up.

ANTENATAL CARE

Review of antenatal clinic cards showed that of the 12 414 patients, 7644 (62%) had been tested for syphilis during pregnancy, 4556 (37%) were not tested, and 214 women had no results indicated on the card and did not know whether the test had been done.

The average gestational age at first booking and testing was 25 weeks and did not differ between clinics. Significantly more women were tested for syphilis in the intervention clinics than in the non-intervention clinics (79% versus 56%, $p<0.001$). Of the 7644 women who had been screened during pregnancy, 228 (3%) were RPR reactive. There was no statistical difference either in RPR reactivity or in the proportion of women treated during pregnancy between intervention and non-intervention clinics. Over 97% of all RPR positive women identified during pregnancy had been treated as well as 75% of the partners. One third of the women were treated after 29 weeks of pregnancy. In 228 (3%) RPR reactive, women had been tested not more than once in pregnancy as recommended by the national guidelines.

Table 1 The different study groups

<table>
<thead>
<tr>
<th>Serological results at delivery</th>
<th>Serological results at antenatal clinic</th>
<th>Treated/not treated</th>
<th>No of women</th>
</tr>
</thead>
<tbody>
<tr>
<td>RPR and TPHA negative (n=275)</td>
<td>RPR negative</td>
<td>Not treated</td>
<td>225</td>
</tr>
<tr>
<td></td>
<td>RPR positive</td>
<td>Treated</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>RPR positive</td>
<td>Treated</td>
<td>88</td>
</tr>
<tr>
<td></td>
<td>RPR positive or negative</td>
<td>Not treated</td>
<td>187</td>
</tr>
</tbody>
</table>


Table 2 Significant odds ratios (OR) obtained from multivariate analysis of risk factors for syphilis seropositivity among women delivering at Pumwani Maternity Hospital

<table>
<thead>
<tr>
<th>Characteristic variable</th>
<th>OR</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 8 years of education</td>
<td>2.3</td>
<td>1.3–4.1</td>
<td>0.007</td>
</tr>
<tr>
<td>History of preterm delivery</td>
<td>2.2</td>
<td>1.0–4.9</td>
<td>0.048</td>
</tr>
<tr>
<td>≥3 antenatal visits</td>
<td>5.1</td>
<td>2.5–10.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Maternal HIV-1 infection</td>
<td>3.3</td>
<td>1.6–6.8</td>
<td>0.001</td>
</tr>
<tr>
<td>More than one sexual partner in past year</td>
<td>6.0</td>
<td>2.8–13.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of genital ulcer disease</td>
<td>12.3</td>
<td>5.1–103.6</td>
<td>0.021</td>
</tr>
</tbody>
</table>

SYPHILIS TESTING AT DELIVERY

RPR testing was done in 12,414 women at delivery. We found 377 (3%) women RPR positive, of whom 296 (79%) were also TPHA positive. The 81 women who were TPHA negative were considered as either early infections or false positive RPRs, and were not invited for further follow up. Of the 296 seroreactive women, 275 (93%) were enrolled. Twenty one women were not available for enrolment owing to early discharge or transfer to other maternity units.

RISK FACTORS FOR SYPHILIS

Univariate analysis of the 275 syphilis seropositive and 275 seronegative controls showed that lower education, being single, having multiple sex partners, a history of STD, a history of preterm delivery, inadequate antenatal care, maternal HIV infection, inadequate antenatal care, maternal HIV infection, and pruritic dermatitis. On multivariate analysis including all significant variables, lower education, history of preterm delivery, inadequate antenatal care, maternal HIV infection, maternal history of preterm delivery, and inadequate antenatal care were significantly and independently associated with syphilis infection. Table 2 shows the statistically significant risk factors for syphilis infection among women in labour at Pumwani Maternity Hospital.

Table 3 Mothers and infant characteristics of the different subgroups

<table>
<thead>
<tr>
<th>Serology at delivery</th>
<th>RPR and TPHA negative (n=275)</th>
<th>RPR and TPHA positive (n=275)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serology antenatal clinic/Rx</td>
<td>RPR(−), Rx(−) (n=223)</td>
<td>RPR(+) Rx(+) (n=50)</td>
</tr>
<tr>
<td>Intervention clinic</td>
<td>35.6%</td>
<td>48.0%</td>
</tr>
<tr>
<td>Birth weight (mean (SD))</td>
<td>3190 (398)</td>
<td>3102 (531)</td>
</tr>
<tr>
<td>Adverse pregnancy outcome</td>
<td>6.2%</td>
<td>8.0%</td>
</tr>
<tr>
<td>Gestation at treatment</td>
<td>RPR−ve (n=50)</td>
<td>RPR−ve (n=88)</td>
</tr>
<tr>
<td>29–40 weeks</td>
<td>16</td>
<td>29</td>
</tr>
<tr>
<td>10–28 weeks</td>
<td>34</td>
<td>50</td>
</tr>
</tbody>
</table>

Figures are percentages or means. *p<0.05 (univariate or with Yates’s correction) for differences between the study group and the control group. Rx = treatment.
Discussion
Our data show that 3% of women delivering at the Pumwani Maternity Hospital were RPR reactive during pregnancy and at delivery. This is lower than the scarce recent prevalence figures reported from other urban sites, but confirms the downward trend of syphilis prevalence among pregnant women delivered in Nairobi. Population differences and selection bias cannot be excluded, but are not likely to play a major part as population characteristics (age, parity, ethnicity, and socioeconomic status) have remained unchanged.

Several hypotheses can be put forward to explain this downward trend—for instance, the likelihood of receiving antibiotic treatment for some intercurrent infection and easier access to antibiotics in an urban area. But equally, one hopes that this positive fact is the consequence of the impact of the prevention and intervention programme on syphilis during pregnancy, changes in health seeking behaviour, and improved health care.

Multivariate analysis of risk factors for maternal syphilis infection at delivery confirmed the predictable fact that syphilis positive women more often showed a risky sexual behaviour, had a lower level of education, inadequate antenatal care, and coexistent HIV infection. This is in line with research findings from Malawi and South Carolina. These sociodemographic risk factors, however, are not very specific for identifying women at high risk, and cannot be used to selectively test women for syphilis. Thus, it is apparent that universal screening (testing) for syphilis in antenatal programmes will remain one of the most appropriate ways to prevent syphilis associated morbidity and mortality.

The finding of high HIV-1 prevalence in both syphilis positive and negative subpopulations of pregnant women is probably an indication of the rapid spread of the HIV pandemic beyond the classic core groups with risky sexual behaviour. This is in contrast with the finding that syphilis prevalence is decreasing in the same population.

Our study confirms the adverse effect of syphilis infection on pregnancy outcome. Mothers who did not receive treatment were four times more likely to have adverse obstetric outcomes. This is lower than the odds ratios found by Hira et al., in Zambia and Wilkinson et al., in South Africa where an overall risk of syphilis related adverse pregnancy outcome of 8.3 and 11.8 respectively, was found. Our study certainly underestimates the impact of syphilis since it was only measured at delivery. Perinatal deaths, occurring 24 hours after the woman had left the maternity ward, were not included. Abortions and home premature births, both adverse outcomes associated with maternal syphilis, were not measured in this study. A cohort study following pregnant women from conception up to delivery and 1 week after can provide the missing information.

A population attributable risk of maternal syphilis as a cause of adverse obstetric outcome of 9% implies that over 90% of stillbirths and low birth weights is not attributed to syphilis infection during pregnancy. Meheus estimated that at 10% of gonorrhoea and 20% of Chlamydia trachomatis prevalence in pregnant women—16% and 9.9% respectively—the high risk of adverse obstetric outcome by two and half times. Our study confirms the adverse effect of treatment such as antibiotics in an urban area. But equally, one hopes that this positive fact is the consequence of the impact of the prevention and intervention programme on syphilis during pregnancy, changes in health seeking behaviour, and improved health care.

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due to the Jarisch-Herxheimer reaction as described by Klein et al., who found an increased risk of preterm delivery and fetal death in a group of 33 pregnant women with syphilis who were monitored after benzathine penicillin therapy. Most of the Jarisch-Herxheimer reactions occurred in women with primary and secondary syphilis and none in those with latent syphilis, probably the most common group in our population under study.

The gestational age at treatment did not seem to have an important effect on pregnancy outcome in our study. Over 30% were treated after 29 weeks with one single dose of benzathine penicillin 2.4 MU as recommended by the national guidelines. However, this observation was based on small numbers out of a population of pregnant women with an average gestational age of 25 weeks at booking. In 1997, Wilkinson et al. showed that intrat uterus death was 19.4 times higher, if no dose or only one dose of penicillin was given, compared with the recommended full course in South Africa of three doses with 1 week interval.

Two recent South African studies recommend rescreening and eventual treatment at the moment of delivery to overcome some of these problems. These studies, however, were carried out in areas with a much higher prevalence than in our study population (9–11%). Further research is needed to study the adverse effect of maternal syphilis on pregnancy outcome. The results show that testing during pregnancy and prompt treatment significantly reduces the rate of low birth weight and stillbirth. On-site testing and treatment have clearly enhanced the coverage of the screening programme and have spilled over from the selected antenatal clinics to the antenatal care sector in Nairobi. The effect of the programme could improve through earlier antenatal attendance, partner notification, and adjustment of treatment protocols. However, the efforts to run the programme are enormous and the public health impact is rather small. Hence, syphilis screening as one of the components of essential obstetric care has to be assessed in different settings in relation to the syphilis prevalence in the population. Alternative interventions such as targeted mass treatment have to be examined in high prevalence areas.

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Contributors: MT developed the proposal, was in charge of monitoring, supervision, and final writing; PG and KC carried out the fieldwork; DK and GK were the field supervisors; JB and KN-A were in charge of the laboratory analyses; LVR did the quality control of the syphilis testing; PC and LA were involved in the statistical analysis, discussion of the results, and assistance in writing the paper.

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