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

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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.*(Sex Transm Inf 2000;76:117-121)*

Keywords: syphilis testing; pregnancy outcome; Kenya

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5 November 1999**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%.¹⁻⁴ 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.^{5,6}Screening and treatment of syphilis during pregnancy is considered to be highly cost effective.⁷ 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 department 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.⁸ 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.⁹

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-

Table 1 The different study groups

Serological results at delivery	Serological results at antenatal clinic	Treated/not treated	No of women
RPR and TPHA negative (n=275)	RPR negative	Not treated	225
	RPR positive	Treated	50
RPR and TPHA positive (n=275)	RPR positive	Treated	88
	RPR positive or negative	Not treated	187

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 immunoassay (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 χ^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. Without exception, women had been tested not more than once in pregnancy as recommended by the national guidelines.

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

Characteristic variable	OR	95% CI	p Value
Less than 8 years of education	2.3	1.3–4.1	0.007
History of preterm delivery	2.2	1.0–4.9	0.048
≤3 antenatal visits	5.1	2.5–10.5	<0.001
Maternal HIV-1 infection	3.3	1.6–6.8	0.001
More than one sexual partner in past year	6.0	2.8–13.0	<0.001
History of genital ulcer disease	12.3	1.5–103.6	0.021

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 negative. 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, and HIV infection were risk factors for syphilis infection. Syphilis seropositive women were also more likely to have a history of alcohol use, to be clinically wasted, to have clinical anaemia, and pruritic dermatitis. On multivariate analysis including all significant variables, lower education, history of preterm delivery, inadequate antenatal care, maternal HIV infection, multiple partners, and a history of genital ulcer disease 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.

SYPHILIS AND ADVERSE OBSTETRIC OUTCOME

Tables 3, 4, and 5 show the impact of syphilis infection and syphilis treatment on pregnancy outcome for the various study groups. Syphilis seropositive women suffered significantly more adverse obstetric outcome than syphilis seronegative women (22.5% versus 6.6%; OR 4.1, $p < 0.001$) (table 4). Women who were syphilis seropositive and untreated were four times more likely to have adverse pregnancy outcomes. The impact of maternal syphilis infection was slightly higher on the incidence of low birth weight (OR 4.0) than on the incidence of stillbirths (OR 3.3) (table 5).

Syphilis treatment during pregnancy reduced the rate of adverse outcome significantly

Table 3 Mothers and infant characteristics of the different subgroups

Serology at delivery	RPR and TPHA negative (n=275)		RPR and TPHA positive (n=275)	
	RPR(-), Rx(-) (n=225)	RPR(+), Rx(+) (n=50)	RPR(+), Rx(+) (n=88)	RPR(+), Rx(-) OR RPR(-), Rx(-) (n=187)
Serology antenatal clinic/Rx	35.6%	48.0%	52.3%*	35.2%*
Adverse pregnancy outcome	6.2%	8.0%	14.7%*	26.2%*
Birth weight (mean (SD))	3190 (538)	3102 (531)	3013 (510)*	2971 (702)*

Figures are percentages or means. * $p < 0.05$ (univariate χ^2 with Yates's correction) for differences between the study group and the control group. Rx = treatment.

Table 4 Obstetric outcome in the two groups, according to maternal syphilis status at delivery

	Syphilis -ve (n=275) (%)	Syphilis +ve (n=275) (%)	Odds ratio	95% CI p value
Adverse obstetric outcome	18 (6.6)	62 (22.5)	4.1	2.3–7.5
No adverse obstetric outcome	255 (93.4)	213 (77.5)		<0.001

Table 5 Pregnancy outcome according to maternal syphilis status at delivery

Outcome	Syphilis -ve	Syphilis +ve	Odds ratio	p Value
Stillbirth	4	13	3.34	0.028
Alive	271	262		
<2500g	14	49	4.01	<0.0001
>2500g	261	226		

Table 6 RPR status at delivery according to the gestation age at treatment

Gestation at treatment	RPR-ve (n=50)	RPR+ve (n=88)	p Value
29–40 weeks	16	29	0.908
10–28 weeks	34	59	

from 26.2% to 14.7%. Women who received treatment during pregnancy and were found syphilis negative at delivery had similar pregnancy outcomes to syphilis seronegative women (8.0% versus 6.2%). However, this group could contain a substantial number of false positives—women who were not syphilis infected but had been treated on the basis of a false positive test and therefore had a similar pregnancy outcome. Women who were treated but were still syphilis positive at delivery had significantly more adverse pregnancy outcome than women without syphilis (14.7% versus 6.2%) but less than untreated women (26.2% versus 14.7%) (table 3).

There was no statistical difference in pregnancy outcome for syphilis positive women in relation to the gestational age at treatment (table 6).

The population attributable risk (PAR) for adverse obstetric outcome due to syphilis infection was 9%. This measurement combines the strength of the risk factor (odds ratio) and the prevalence of the risk factor in the population.¹ The PAR for infected women who were treated went down to 3%.

The HIV seroprevalence among syphilis positive mothers was 26% compared with 11% among syphilis negative mothers ($p < 0.001$). Syphilis seropositivity was significantly associated with HIV infection.

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,^{5 6 10-12} but confirms the downward trend of syphilis prevalence among pregnant women delivering in Nairobi.^{13 14} Population differences and selection bias cannot be excluded, but are not likely to play a major part as population characteristics (age, parity, ethnicity, and socio-economic 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.^{7 10} 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 Zambia⁶ and Wilkinson *et al*, in South Africa¹⁵ 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,¹⁶ 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, of prematurity can be attributed to these infections¹⁷ HIV infection is one of the other studied risk factors for adverse fetal outcome. Temmerman *et al* found an odds ratio of 2.5 for low birth weight and stillbirth. Applied to this population, with an HIV seroprevalence of 15.9% the population attributable risk of HIV infection as a cause of adverse obstetric outcome is 19%.^{13 18}

Hence, a perfectly functioning syphilis screening and treatment programme would have rather a minimal public health impact in this population with its decreasing syphilis prevalence.¹⁴ On an individual basis, however, the high risk of adverse obstetric outcome associated with syphilis infection still justifies the need to control syphilis in pregnancy.

Our results show that significantly more women were screened in the 10 intervention clinics as compared with the non-intervention clinics. On the other hand, 56% of pregnant women attending the non-intervention clinics were also screened. Before 1995, only 9% of pregnant women infected with syphilis received treatment.⁸ The unexpected finding that there were no differences in the proportion of women treated in intervention and non-intervention clinics is encouraging. This suggests that the effect of the decentralised RPR screening and syphilis treatment seems to spread to other clinics, without deliberate strategy. Probably this spillover effect of the intervention could be explained by the practice that women attending non-intervention clinics are referred to intervention clinics for screening and treatment. The improved situation could also be the consequence of staff posting whereby nurses trained in the intervention clinics can be transferred to non-intervention clinics and carry on with their good practice. This might be one of the contributing factors for the decreasing syphilis seroreactivity in this population.

Syphilis testing and prompt treatment have been shown to prevent adverse obstetric outcome related to syphilis.^{6 15 17} This is confirmed by our data indicating that women who were RPR reactive, treated, and RPR negative at delivery had similar pregnancy outcome to the non-RPR reactive women. Women who were reactive and treated during pregnancy but who were still RPR reactive at delivery had worse outcomes than the non-infected women. Treatment reduced the rate of adverse obstetric outcome by two and half times. Our results suggest that treatment of syphilis RPR reactivity during pregnancy for women who were still RPR reactive at delivery did not bring the level of adverse pregnancy outcome down to that of non-infected mothers. It is possible that in our study, mothers who were RPR reactive and were treated became reinfected before delivery. Moreover, other factors are important in reducing the effect of treatment such as inadequate treatment, treatment too late in pregnancy, or reinfection.¹⁹ In addition, some of the preterm deliveries or stillbirths may be

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.²⁰ 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 intrauterine 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.¹⁵ Two recent South African studies recommend rescreening and eventual treatment at the moment of delivery to overcome some of these problems.^{21 22} 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 chances of being infected during pregnancy, and to determine optimal treatment schedules.

In conclusion, our study confirms 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.

This work is supported by the European Commission, DG VIII, A2, Health-Aids Population Unit, Social Human and Cultural Development; Gender through grant 7RPR-28 KE.

Contributors: MT developed the proposal, was in charge of monitoring, supervision, and final writing; PG and KF carried out the fieldwork; DK and GK were the field supervisors; JB and JN-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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