Maternal and congenital syphilis in Bolivia, 1996: prevalence and risk factors

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Objectives The present study was carried out in seven maternity hospitals to determine the prevalence of maternal syphilis at the time of delivery and the associated risk factors, to conduct a pilot project of rapid syphilis testing in hospital laboratories, to assure the quality of syphilis testing, and to determine the rate of congenital syphilis in infants born to women with syphilis at the time of delivery — all of which would provide baseline data for a national prevention programme in Bolivia.

Methods All women delivering either live-born or stillborn infants in the seven participating hospitals in and around La Paz, El Alto, and Cochabamba between June and November 1996 were eligible for enrolment in the study.

Findings A total of 61 out of 1428 mothers (4.3%) of live-born infants and 11 out of 43 mothers (26%) of stillborn infants were found to have syphilis at delivery. Multivariate analysis showed that women with live-born infants who had less than secondary-level education, who did not watch television during the week before delivery (this was used as an indicator of socioeconomic status), who had a previous history of syphilis, or who had more than one partner during the pregnancy were at increased risk of syphilis. While 76% of the study population had received prenatal care, only 17% had syphilis testing carried out during the pregnancy; 91% of serum samples that were reactive to rapid plasma reagin (RPR) tests were also reactive to fluorescent treponemal antibody-absorption (FTA-ABS) testing. There was 96% agreement between the results from local hospital laboratories and national reference laboratories in their testing of RPR reactivity of serum samples. Congenital syphilis infection was confirmed by laboratory tests in 15% of 66 infants born to women with positive RPR and FTA-ABS testing.

Conclusion These results indicate that a congenital syphilis prevention programme in Bolivia could substantially reduce adverse infant outcomes due to this disease.

Keywords: syphilis, congenital, prevention and control; syphilis, congenital, epidemiology; fetal death; infant mortality; pregnancy complications; syphilis serodiagnosis; fluorescent treponemal antibody-absorption test; Bolivia.

Mots clés: syphilis congénitale, lutte; syphilis congénitale, épidémiologie; syphilis, sérodiagnostic; mort fœtale; mortalité du nourrisson; complications de la grossesse, diagnostic; test FTA-ABS; facteurs socio-économiques; Bolivie.

Palabras clave: sífilis congénita, prevención y control; sífilis congénita, epidemología; muerte fetal; mortalidad infantil; complicaciones infecciosas del embarazo, diagnóstico; serodiagnóstico de la sífilis; test de absorción del anticuerpo fluorescente de treponema; factores socioeconómicos; Bolivia.

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Introduction

Much attention and considerable resources are being focused on limiting the vertical transmission of human immunodeficiency virus (HIV) infection from pregnant women to their infants (*1*). At the same time, it is essential for public health programmes not to neglect the prevention of another congenital infection, namely congenital syphilis. This is a potentially devastating condition that can cause fetal death, prematurity, meningitis, vasculitis, bone and joint destruction, and multi-system disease (*2*). Studies in the pre-penicillin era demonstrated that a woman with primary or secondary syphilis had a 70% or greater chance of infecting her fetus (*3*). More recently it was reported that 30–60% of infected live-born infants show no signs of congenital syphilis at birth (*4*). Penicillin treatment is effective for both the pregnant woman and the fetus if given a sufficient time before birth (*3*).

Congenital syphilis causes a large burden of disease in resource-poor settings (*5*). For example, a

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study in Zambia reported that almost 1% of infants born in a major university hospital in Lusaka had signs of congenital syphilis at delivery (*6*). Also, a recent population-based study in Malawi showed that 26% of stillbirths, 11% of neonatal deaths, 5% of post-neonatal deaths, and 8% of infant deaths were attributable to active maternal syphilis infection (*7*).

Maternal syphilis is also a significant problem in South America. Several studies during the 1990s in Central and South America showed reactive syphilis tests in pregnant women ranging from 1.7% in Panama to 11.5% in Recife, Brazil (*8*). Consequently, in 1995, the Pan American Health Organization (PAHO) began a campaign to reduce the rate of congenital syphilis in the Americas to 0.5 (or fewer) cases per 1000 live births by increasing the coverage of antenatal care, establishing routine syphilis serology testing during prenatal care and at delivery, and promoting diagnostic strategies to ensure rapid treatment of infected pregnant women (*8*).

In Bolivia, neonatologists and hospital-based paediatricians have reported anecdotally that congenital syphilis is a common problem, but few data are available. In 1994, the prevalence of symptomatic congenital syphilis reported to the Bolivian Ministry of Health was 3.1 per 1000 live births (*9*). However, this may be an underestimate because a study during the early 1990s reported that 10.9% of 892 women who gave birth in the German Urquidi maternity hospital in Cochabamba had a reactive VDRL test (F. Torrico, unpublished data, 1993). At the time of the present study, the Bolivian Ministry of Health recommended routine syphilis testing during pregnancy. However, funds and services for such testing were not provided, and the recommendation was not widely followed.

The present study's objectives were as follows: 1) to determine the prevalence of syphilis in women giving birth in Bolivian maternity hospitals and the associated risk factors; 2) to conduct a pilot project on rapid plasma reagin (RPR) testing at the time of delivery; 3) to assure the quality of syphilis serological testing; and 4) to determine the rate of congenital syphilis in infants born to women with maternal syphilis at delivery.

The results of this investigation were used as a baseline to develop a national congenital syphilis prevention programme.

Materials and methods

All women delivering either live-born or stillborn infants in the seven participating hospitals in and around La Paz, El Alto, and Cochabamba between June and November 1996 were eligible for enrolment in this investigation. The study was approved by the Bolivian Ministry of Health and Social Welfare, the participating local institutions, the Office for Protection from Research Risks of the National Institutes of Health, and the institutional review board of the Centers for Disease Control and Prevention (CDC) in the USA. Each participating woman was required to give her written informed consent. A standardized antenatal and obstetrics form and a short questionnaire on risk factors were filled out for each woman. Venous blood samples were obtained from the women, while from infants samples of blood were collected by venepuncture or from heel stick. A 2-cm length of the umbilical cord was taken from the portion closest to the infant at birth and immediately placed in 10% formalin.

The women and their infants were given syphilis treatment before discharge if the mother's serum was reactive to the RPR test carried out in the hospital laboratory at the time of delivery (*10*), and if there was no record in either the mother's medical notes or antenatal card (a standard card given to every pregnant woman who receives antenatal care in Bolivia) that adequate penicillin treatment had previously been given — in accord with CDC treatment guidelines — during the pregnancy at least 30 days before the delivery (*11*) Treatment for syphilis, based on CDC treatment guidelines, was begun for both infected mothers and infants prior to their discharge from hospital (*11*). A full course of treatment at home was arranged for infants who did not require hospitalization and were discharged. If any women or infants had inadvertently been discharged before receiving treatment, a trained individual was sent to find them in their homes, explain the treatment, and administer penicillin. Before the study began, the individual hospitals were asked to develop their own strategies for partner notification and treatment. During the study, women with reactive RPR tests were asked to assist with the notification of their partner(s).

Participation rates in all hospitals where women gave birth to either live-born or stillborn infants were determined by inspection of birth registers or hospitalization registers. Their clinical records were also reviewed.

Case definitions

A woman was considered to have maternal syphilis if her serum at the time of delivery was reactive to the RPR test and fluorescent treponemal antibody-absorption (FTA–ABS) test, as carried out by the Bolivian reference laboratories, and if there was no written record that she had received adequate treatment for syphilis during the pregnancy and at least 30 days before delivery.

An infant was considered to have laboratory-confirmed congenital syphilis if he or she was born to a woman with maternal syphilis and also if any one of the following was positive: direct fluorescent antibody (DFA) test, immunohistochemistry, or IgM western blot assay.

Laboratory tests

Extensive laboratory preparation was undertaken to ensure the quality of the syphilis serological test results. The Bolivian reference laboratories were

selected based on their performance of analysing sera of known syphilis reactivity prepared by CDC. Before the study, a CDC-trained microbiologist visited each participating hospital laboratory and trained the staff on qualitative and quantitative RPR testing. During the study, the same microbiologist returned to each hospital to review the RPR testing techniques.

Qualitative and quantitative RPR tests were performed on maternal serum samples in the hospital laboratory using a standardized procedure (*10*), and the results were given to clinicians before the woman was discharged. The sera were sent from the hospitals to one of two Bolivian reference laboratories. Since one of the participating hospitals did not have a functioning laboratory, all the tests for that hospital were carried out by the Bolivian reference laboratory, which was next door to the hospital. The reference laboratories performed qualitative and quantitative RPR tests on all the maternal serum samples. FTA-ABS assay was performed on all RPR-reactive sera and also on 2% of non-reactive sera (*10*). A minimally reactive FTA-ABS was designated as non-reactive. Individuals performing the analyses in the Bolivian reference laboratories were not provided with the hospital laboratory results.

For establishing quality assurance, the maternal and infant serum samples and umbilical cord specimens from both the pilot and the actual study participants were sent to CDC in Atlanta, GA, USA where the RPR and FTA-ABS tests were performed on all RPR and/or FTA-ABS reactive maternal sera and on a systematic 10% sample of non-reactive sera from the Bolivian reference laboratories. In the few cases where the Bolivian reference laboratories had diagnosed a woman to be non-reactive and CDC diagnosed the woman as having a reactive RPR and FTA-ABS test, the results were sent to the Bolivian investigators who then contacted the woman in order to start treatment. Serum samples from the infants of the women tested had the following analyses performed at CDC: qualitative and quantitative RPR tests, microhaemagglutination *Treponema pallidum* (MHA-TP) test (*10*), IgM ELISA (*12*), and IgM western blot (*13*) assays. The individuals performing the analyses at CDC were not provided with the earlier test results. Because only a small percentage of the maternal sera was tested by CDC, all analyses of risk factors and outcomes were based on the test results from the Bolivian reference laboratories.

From the group of infants described above, a subset was chosen for analysis of umbilical cord specimens at CDC — comprising all umbilical cords from the infants of women with presumptive maternal syphilis and a random sample of cords from infants born to women without syphilis. In addition, the formalin-fixed umbilical cords from the infants of six women with syphilis identified during the initial pilot study of 88 women were included and the DFA test (*10*) and immunohistochemistry (*14*) were performed on them.

Statistical analysis

Univariate analysis was carried out using the χ^2 test or Fisher's exact test (if the expected cell values were less than 5). Median values of continuous variables were compared using nonparametric tests. Backwards stepwise logistic regression was used for multivariate analysis (SAS Institute, Cary, NC, USA). The chunk test was used to evaluate interaction terms (*15*).

Results

Characteristics of the participants

The overall participation rate in all seven hospitals for women giving birth to live-born infants was 63% (1428/2264). Hospital-specific participation rates varied from 54% in one of the large referral maternity hospitals to 93% in one of the small hospitals. Information on antenatal history was available for 1368 (96%) of 1428 women with live-born infants; of these, 1043 (76%) received antenatal care, but only 227 (17%) had a record of having been tested for syphilis during pregnancy. A total of 210 women who gave birth to live-born infants reportedly had a negative VDRL test during pregnancy; 7 women had documentation of VDRL testing but no results were available, and 10 women had a record of a reactive VDRL test during pregnancy.

Of the 325 women who did not receive antenatal care, 75 (23%) said they did not seek it because they were afraid of the doctor and medical services, 73 (22%) thought that antenatal care was not important, 65 (20%) said they lacked money to pay for such care, 60 (18%) said they did not live close enough to the antenatal care services, 47 (14%) reported that they could not leave their work, 24 (7%) said they had no one to watch over their children, and 14 (4%) said that they had no transport. The women could indicate more than one response.

During the recruitment period, four hospitals reported the delivery of stillborn infants. The three hospitals with the fewest deliveries reported no stillbirths during the study period. Of a total of 95 women with stillborn infants, 43 (45%) were enrolled in the study. The median gestational age of the stillborn infants was 37.5 weeks (range, 24–42 weeks), and the median birth weight was 2200 g (range, 400–3950 g). The median birth weight and median gestational age of stillborn infants were less than those of live-born infants (2200 g vs 3240 g, $P = 0.003$; 37.5 weeks vs 40 weeks, $P = 0.006$).

The characteristics of the mothers of live-born and stillborn infants were similar with respect to their income, the urban/rural location of their homes, the number of previous pregnancies and births, and the number and educational level of their partners during pregnancy (Table 1 and Table 2). However, the mothers of stillborn infants were more likely to be older, to speak an indigenous language rather than Spanish at home, to have less education, and to have maternal syphilis at the time of delivery.

Table 1. **Characteristics of women with an RPR test obtained at the time of delivery who had live-born or stillborn infants in seven Bolivian maternity hospitals, 1996**

Characteristic[a]	No. of women with live-born infants	No. of women with stillborn infants	*P*-value
Location of home			
Urban	1049 (79)[b]	23 (72)	
Rural	284 (21)	9 (28)	0.5
Age (years)			
< 20	286 (21)	7 (22)	
20–29	746 (55)	9 (28)	
⩾30	333 (24)	16 (50)	0.002
Preferred language at home			
Spanish	675 (49)	12 (35)	
Aymara	291 (21)	15 (44)	
Quechua	414 (30)	7 (21)	0.006
Educational level			
None	99 (7)	7 (23)	
Primary	554 (41)	13 (43)	
Secondary	635 (47)	10 (33)	
University	52 (4)	0 (0)	0.007
Received antenatal care			
Yes	1043 (76)	20 (61)	
No	325 (24)	13 (39)	0.06
Maternal syphilis at delivery			
Yes	61 (4)	11 (26)	
No	1367 (96)	32 (74)	0.001
History of syphilis			
Yes	26 (2)	0 (0)	
No	1309 (98)	34 (100)	1.0
Watched television in the previous week			
Yes	1098 (80)	26 (77)	
No	283 (20)	8 (23)	0.8
Listened to the radio during the previous week			
Yes	1031 (75)	22 (65)	0.3
No	350 (25)	12 (35)	
Income less than the median monthly household (350 Bolivianos = US$ 70)			
Yes	595 (49)	16 (50)	
No	621 (51)	16 (50)	1.0
No. of partners during pregnancy			
None	200 (17)	7 (25)	
One	968 (83)	21 (75)	
More than one	3 (<1)	0 (0)	0.5
Had a steady partner at the time of delivery			
Yes	1141 (82)	27 (82)	0.9
No	244 (18)	6 (18)	
Educational level of steady partner			
Less than secondary	497 (44)	17 (63)	0.1
Secondary or more	524 (47)	7 (26)	
Don't know	106 (9)	3 (11)	

[a] Individuals with unknown values were excluded.

[b] Figures in parentheses are percentages for each category.

Non-participating women

The characteristics of the participating and non-participating women with live-born infants are shown in Table 3. Clinical information was available for 44 (85%) of the 52 mothers of stillborn infants who did not participate in the study. There were no significant differences in the proportions with low birth weight (<2500 g) and prematurity (<37 weeks) between the stillborn infants whose mothers did or did not participate in the study.

Laboratory results

Repeat tests performed for quality assurance generally showed a high level of agreement between the local hospital results and the national reference laboratory results. Of the 847 samples analysed by both a hospital laboratory and the Bolivian reference laboratory, there was 96% agreement for the qualitative RPR results. One small hospital laboratory accounted for 44% of the discrepant results. Of the 37 samples analysed by hospital laboratories and by CDC, there was 97% agreement on the qualitative RPR results. Qualitative RPR testing was carried out on the sera from 166 women by both a Bolivian reference laboratory and CDC, with 96% agreement (159/166). FTA-ABS testing was carried out on the sera from 78 women by both a Bolivian reference laboratory and the CDC laboratory, with 94% agreement.

Confirmatory testing of the hospital laboratories' RPR results by the Bolivian reference laboratories showed that only a small proportion was false-positive. Of 80 specimens that were RPR reactive at the Bolivian reference laboratory, 73 (91%) had reactive FTA-ABS results. Of the 73 specimens with a reactive RPR and FTA-ABS, 62% had a titre of =1:8. The median titre of these 73 specimens was 1:16 (range, 1:1 to 1:256), compared with a median titre of 1:2 (range 1:1 to 1:16) for the 7 specimens that were RPR reactive and FTA-ABS non-reactive.

The umbilical cords from 66 infants born to women with presumptive syphilis at delivery were analysed at CDC; 57 of these infants were born alive, 6 were stillborn, and the status of 3 at birth was not known. Of the 66 infants born to women with syphilis, 10 (15%) could be confirmed as having congenital syphilis by immunohistochemistry or DFA testing of the umbilical cord, or by IgM western blot assay of the infants' sera. Of these 10 children, 8 were born alive and 2 were stillborn.

Comparison of women with and without maternal syphilis

A total of 61 (4.3%) out of 1428 mothers of live-born infants in the seven different hospitals were diagnosed with maternal syphilis (median, 4.5%; range, 2.7–6.4%; $P = 0.3$); there were no statistically significant differences in syphilis prevalence between the hospital sites. Physical signs were neither sensitive nor specific for maternal syphilis; upon being

examined, only 3 (5%) out of 61 women with syphilis had physical signs indicative of syphilis (rash, condyloma latum, mucous patches on the tongue, or a genital ulcer), compared with 39 (3%) out of 1367 women without syphilis (relative risk (RR) = 1.6; 95% confidence interval (CI) = 0.5–5.0).

Of the 10 women with live-born infants and documented reactive VDRL tests during pregnancy, only 4 had a record of treatment for syphilis in their antenatal files. A total of 49 of 61 (80%) women with live-born infants who were diagnosed with syphilis at the time of delivery had a record of receiving adequate treatment: 38 of the women with live-born infants had received their treatment in the hospital at the time of delivery. Of the 11 women with syphilis who gave birth to stillborn infants, 10 (91%) had received treatment, 8 of them in the hospital at the time of delivery. Of the 210 women with a non-reactive VDRL test during pregnancy recorded on their antenatal files, 6 had reactive RPR and FTA results at the time of delivery.

Bivariate analysis showed that women with live-born infants were at increased risk of maternal syphilis if they spoke an indigenous language rather than Spanish at home, had no antenatal care, had less than a secondary school education, had a history of syphilis, had a monthly household income less than the median (US$ 70), had more than one partner during the pregnancy or had a partner with less than a secondary school education (Table 4). Several of these variables were highly correlated. For example, compared with women who watched television in the week before delivery, those who did not watch television were less likely to have received antenatal care (66% vs 79%; $P<0.001$), to have an income less than the median of the study population (63% vs 45%; $P<0.001$), or to have had a secondary education (72% vs 43%; $P<0.001$). In a multivariate analysis, four variables were independently associated with maternal syphilis (Table 5). Interaction terms did not contribute significantly to the model.

Table 2. **Summary characteristics of women with an RPR test obtained at the time of delivery who had live-born or stillborn infants in seven Bolivian maternity hospitals, 1996**

Characteristic	Women with live-born infants		Women with stillborn infants		*P*-value
	Median	Interquartile range	Median	Interquartile range	
Age (years)	23	20–29	29	21–34	0.07
Monthly income (US$)	70	50–100	65	30–85	0.92
No. of previous pregnancies	1	0–3	3	0–5	0.11
No. of previous births	1	0–3	2	0–4	0.19

Table 3. **Characteristics of women who did and did not participate in RPR testing at the time of delivery, and of their live-born infants in seven Bolivian maternity hospitals, 1996**

Characteristic	Participating women		Non-participating women		*P*-value
	Median	Interquartile range	Median	Interquartile range	
Age at delivery (years)	23	20–29	24	20–29	0.2
No. of pregnancies	1	0–3	2	1–4	0.001
Gestational age of infant (weeks)	40	39–40	39	37–40	0.001
Birthweightofinfant(g)	3240	2940–3540	3180	2810–3450	0.005
% who received antenatal care	76		57		0.001
% who gave birth to a low-birth-weight infant	7		12		0.001
% who gave birth to a premature infant			16		0.001

Characteristics of live-born infants

Women with syphilis who gave birth to live-born infants were more likely than women without syphilis to have a low-birth-weight infant (16% vs 7%, OR = 2.6, 95% CI = 1.2–4.8). However, there was no significant difference between the proportions of premature live-born infants born to women with and without syphilis (5% vs 4%, OR = 1.2, 95% CI = 0.3–4.3). A total of 23 (1.6%) out of 1428 live-born infants had physical signs that could be compatible with syphilis (sero-sanguineous nasal discharge, skin eruptions, hepatosplenomegaly, or jaundice); 5% of the live-born infants of women with syphilis had physical signs at birth, while only 1.5% of live-born infants of women without syphilis had such physical signs (RR = 3.2, 95% CI = 1.1–9.4). Women with signs compatible with early syphilis (genital ulcers, body rash, condyloma lata, or mucous patches on the tongue) were more likely to have live-born infants with physical signs compatible with syphilis than women who did not have such signs (7% vs 1%, RR = 5.0, 95% CI = 1.5–16.0). Adequate treatment for congenital syphilis was received by 50 infants (82%) and 12 (20%) of 61 of the live-born infants had all their treatment at home.

Maternal and infant risk factors for laboratory-confirmed congenital syphilis

Significant differences existed between the women with syphilis who had infants with and without confirmed congenital syphilis. Women with syphilis at delivery and with physical signs compatible with syphilis were more likely to give birth to an infant with laboratory-confirmed congenital syphilis than those who did not have physical signs (67% vs 11%, OR = 16.7, 95% CI = 1.0–555.6; $P = 0.05$). Of the 7 women whose infants had confirmed congenital syphilis and for whom physical examination results were available,

Table 4. **Comparison between Bolivian women giving birth to live-born infants who had and did not have maternal syphilis at the time of delivery, 1996**

Characteristic[a]	No. of women	No. with maternal syphilis at delivery	Relative risk/ 95% confidence interval[b]
Location of home			
Urban	1049	42 (4.0)[c]	0.7/0.4–1.3
Rural	284	16 (5.6)	
Age (years)			
< 20	286	12 (4.2)	1.0/0.5–1.8
⩾ 20	1079	47 (4.4)	
Preferred language at home			
Indigenous	705	41 (5.8)	2.1/1.2–3.5
Spanish	675	19 (2.8)	
Less than secondary education			
Yes	653	46 (7.0)	3.7/2.0–6.8
No	687	13 (1.9)	
Received antenatal care			
Yes	1043	38 (3.6)	0.5/0.3–0.9
No	325	22 (6.8)	
History of syphilis			
Yes	26	4 (15.0)	3.6/1.4–9.2
No	1309	56 (4.3)	
Watched television during the previous week			
Yes	1098	37 (3.4)	0.4/0.3–0.7
No	283	23 (8.1)	
No. of partners during pregnancy			
More than one	3	1 (33.3)	7.5/1.5–38.7
None or one	1168	51 (4.4)	
Had steady partner at time of delivery			
Yes	1141	47 (4.1)	0.8/0.4–1.4
No	244	13 (5.3)	
Steady partner had less than secondary education			
Yes	497	28 (5.6)	2.7/1.4–5.4
No	524	11 (2.1)	
Income less than median weekly household income (US$ 70):			
Yes	595	36 (6.1)	2.0/1.2–3.4
No	621	19 (3.1)	

[a] Individuals with unknown values excluded.

[b] Values shown are for the reference group.

[c] Figures in parentheses are percentages.

two had condyloma lata at delivery. The women with syphilis whose infants had confirmed congenital syphilis had higher geometric mean RPR titres than the women with syphilis whose infants did not have confirmed congenital syphilis (1:32 vs 1:12; $P = 0.001$). They were also less likely to have a stable partner at the time of delivery (10% vs 44%, OR = 0.1, 95% CI = 0.0–0.9). There were no significant differences between the two groups with respect to the preferred language at home (Spanish vs indigenous), educational level less than secondary, antenatal care attendance, rural/urban residence, and age.

There were also differences between the infants with and without laboratory-confirmed congenital syphilis born to women with syphilis at delivery. Infants with confirmed congenital syphilis were more likely to be low birth weight (<2500 g) than infants of women with syphilis without laboratory-confirmed congenital syphilis (78% vs 14%, OR = 22, 95% CI = 3.1–197.3) and to be premature (<37 weeks gestation) (50% vs 4%, OR = 24, 95% CI = 2.5–287.7). None of the six live-born infants with laboratory-confirmed congenital syphilis, for whom physical examination data were available at birth, had physical signs indicative of syphilis (hepatosplenomegaly, rash, sero-sanguineous nasal discharge, or jaundice). The two stillborn infants with confirmed congenital syphilis were born macerated.

Discussion

Innovative approaches for the diagnosis and treatment of maternal syphilis, such as the on-site testing and treatment plan carried out in this study, have been documented in several resource-poor settings. In Zambia, for example, an on-site syphilis screening and treatment programme reduced by two-thirds the adverse outcomes attributable to syphilis (*16*). A Kenyan programme, also with an on-site testing and treatment strategy, screened a total of 13 131 women and documented a 6.5% prevalence of RPR test reactivity. The investigators calculated that 413 cases of congenital syphilis were prevented at a cost of US$ 50 per case prevented (*17*). Specific cost-effectiveness studies have not been carried out in Bolivia, but other reports have described the cost-effectiveness of antenatal syphilis testing programmes even in areas with low syphilis seroprevalence (*18,19*). The implementation of these strategies is feasible in countries that have limited medical and laboratory facilities, such as Bolivia.

A broad-based maternal syphilis prevention programme, using on-site testing and treatment, would improve maternal and infant health in Bolivia. The present study showed a high prevalence of maternal syphilis, 4% in women giving birth to live-born infants and 26% in women with stillborn infants in several Bolivian hospitals. Having either a known history of syphilis or more than one partner during pregnancy was a strong risk factor for maternal syphilis at delivery. However, these characteristics were uncommon and present in fewer than 50% of women with syphilis at delivery. Therefore, if only these characteristics were used to screen women, more than one half of the cases of maternal syphilis would be missed.

The other two risk factors for maternal syphilis at delivery, i.e. lack of secondary education and not

having a television to watch during the week before delivery (as an indicator of socioeconomic status), were highly prevalent in the study population; this is also true for the country as a whole. According to the 1994 National Health and Demographic Survey of Bolivia, 63% of Bolivian women aged 15–44 years had less than a secondary education and 33% of Bolivian women did not watch television at least once weekly (*20*). However, the prevalence of maternal syphilis was still substantial even in women without these risk factors.

Antenatal care as currently practised in Bolivia appears to have been minimally effective in reducing the risk of maternal syphilis in women who give birth in hospitals. Although the majority of the participating mothers received antenatal care, only a minority had documented proof that a syphilis test had been performed during the pregnancy. More women may have had undocumented screening and treatment during pregnancy. However, discussions with hospital physicians suggest that pregnant women are not routinely screened. These physicians reported that they know these women ought to be screened for syphilis during pregnancy, but that the obstacle for most women is the cost. At the time of the study, pregnant women had to pay for both syphilis testing and treatment. Antenatal care providers usually do not recommend a syphilis test if they believe that the woman has no risk behaviour for sexually transmitted diseases (Ilanes, personal communication, 1996).

This study demonstrates that a syphilis screening programme for pregnant women in Bolivia is feasible. The high rate of agreement between the RPR results from the hospital laboratories and those of both the Bolivian reference laboratories and CDC showed that accurate RPR tests can be carried out on-site with minimal training of local staff in decentralized locations with basic facilities. The study also showed that the percentage of pregnant women with false-positive RPR results was small. Clinicians can be confident that a pregnant woman with a reactive RPR has a high probability of having syphilis. The low rate of false-positive RPR results alleviates the need for routine confirmatory testing, which is prohibitively expensive for most women and not available in most settings.

The investigation's laboratory data together with information collected from pre-existing antenatal records suggest that some women may seroconvert from a negative to a reactive syphilis test between an initial test during antenatal care and testing at the time of delivery. However, we cannot assess the quality of VDRL testing during pregnancy because these were done independently of our study; it is therefore not possible to state for certain that these women actually had seroconversions during pregnancy. At present, we cannot make any specific recommendations about testing each woman twice for syphilis during pregnancy in Bolivia. It is nevertheless essential to ensure treatment of all asymptomatic infants of RPR-reactive mothers at birth. Our study showed that six live-born infants with laboratory-confirmed congenital syphilis were asymptomatic at birth. Therefore, all newborn infants of women with reactive syphilis tests, including asymptomatic infants, require immediate penicillin therapy.

Table 5. **Multivariate analysis of risk factors associated with syphilis at the time of delivery in Bolivian women with live-born infants, 1996**

Characteristic[a]	Total number	No. with syphilis	Odds ratio/ 95% confidence interval[b]
Less than secondary education			
Yes	653 (49)[c]	46 (7.0)	3.1/1.6–6.2
No	687 (51)	13 (1.9)	
Watched television during past week			
Yes	1098 (80)	37 (3.4)	0.5/0.3–0.9
No	283 (20)	23 (8.1)	
History of syphilis			
Yes	26 (<1)	4 (15.0)	6.7/2.1–21.7
No	1309 (99.9)	56 (4.3)	
No. of partners during the pregnancy			
More than one	3 (<1)	1 (33.3)	28.5/2.4–339.4
One or none	1168 (99)	51 (4.3)	

[a] Unknown values excluded.

[b] Values shown are for the reference group.

[c] Figures in parentheses are percentages.

This study had several limitations: it only included women who gave birth in hospitals, which is estimated to be approximately 60% of Bolivian women who give birth (*20*). Furthermore, the participation rate of mothers was low in some of the hospitals. It is likely that the prevalence of syphilis in pregnant women found by this study underestimated the actual prevalence in such women attending these hospitals. Compared with women who participated in the investigation, the women who gave birth in the study hospitals and who did not participate were more likely to have a low-birth-weight infant and a small-for-gestational-age infant. It is known that syphilis is a cause of premature birth (*2, 3*), and the hospital staff may not have had the time to enrol women and collect samples during emergency or urgent deliveries. Furthermore, the women who participated may have been at lower risk for syphilis than the general Bolivian population of women of child-bearing age. According to the Bolivian National Demographic and Health Survey in 1994 (*20*), 53% of pregnant Bolivian women received antenatal care, compared with 76% of the study participants, and 37% of Bolivian women of child-bearing age had at least a secondary school education, compared with 51% of the study population.

The study probably also underestimated the prevalence of congenital syphilis in infants born to women with syphilis. The sensitivity of IgM tests for treponemal antibody in asymptomatic congenital syphilis or in babies infected late in pregnancy is

unknown, and not all of the babies born to women with syphilis had serum available for testing. Also, the sensitivity and specificity of the immunohistochemistry results were unknown. The immunohistochemistry results were reported as positive only if whole spirochaetes were visualized. Four of the umbilical cords from infants of women with syphilis showed antigenic material that could have been treponemal fragments. While the fragments were considered highly suspicious for congenital syphilis, their exact significance was not known.

Based on these results, we recommend the following measures for the control and prevention of maternal syphilis in Bolivia, as well as in other countries with substantial rates of this disease:

- coverage and utilization of antenatal care by pregnant women must be increased; all women should receive free antenatal syphilis testing (providing free or subsidized syphilis testing and treatment is essential to remove cost barriers for pregnant women with limited means — it is far preferable to test for syphilis early during antenatal care than to test for syphilis only at the time of delivery);
- antenatal care providers and maternity hospital staff members in Bolivia must be taught that syphilis is common and that, in such settings, confirmatory serological testing is not necessary for treatment based on a presumptive diagnosis;
- on-site testing is essential so that women can be tested and receive the results during the same visit to ensure prompt treatment, otherwise women may be lost to follow-up;
- any pregnant woman who has a reactive RPR test result without documentation of adequate penicillin therapy earlier during the pregnancy (according to Ministry of Health and Social Welfare guidelines) should be given immediate penicillin treatment;
- any infant born to a woman with syphilis diagnosed at the time of delivery should be treated with penicillin, regardless of the presence or absence of physical symptoms;
- culturally appropriate partner notification techniques, which are sensitive to domestic relationships, need to be developed;
- a functional reporting system should be established to notify the Ministry of Health and Social Welfare of all cases of maternal syphilis and congenital syphilis in order to improve the monitoring of syphilis cases and trends.

As a result of this study, a national congenital syphilis prevention programme providing universal on-site testing of pregnant and parturient women was developed. In December 1998, a ministerial order was passed which decreed that all pregnant women in Bolivia can receive free basic antenatal care, including routine syphilis testing during antenatal care and again at the time of delivery, as well as free penicillin treatment for the mother, her partner, and the infant. Specific cost-effectiveness studies have not been carried out in Bolivia, but the total cost of each syphilis test is US$ 0.70 and is provided through municipal funds. Beginning in July 1999, routine free antenatal syphilis testing has been implemented in a number of Bolivian clinics and hospitals. ■

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Résumé

Syphilis maternelle et congénitale en Bolivie, 1996 : prévalence et facteurs de risque

Objectif La présente étude a été réalisée dans sept maternités en vue de déterminer la prévalence de la syphilis maternelle au moment de l'accouchement et les facteurs de risque associés, d'entreprendre un projet pilote de dépistage rapide de la syphilis dans les laboratoires hospitaliers, d'assurer la qualité des tests

sérologiques et de déterminer le taux de syphilis congénitale chez les nourrissons dont la mère était atteinte de syphilis au moment de l'accouchement, tous éléments qui constitueront les données de base d'un programme national de prévention en Bolivie.

Méthodes Toutes les femmes ayant mis au monde un enfant vivant ou mort-né dans les sept hôpitaux participants à La Paz, El Alto et Cochabamba, ou à proximité, entre juin et novembre 1996 répondaient aux critères de recrutement de l'étude.

Résultats Au total, 61 mères sur 1428 (4,3 %) ayant donné naissance à un enfant vivant et 11 mères sur 43 (26 %) ayant eu un enfant mort-né étaient atteintes de syphilis au moment de l'accouchement. Une analyse multivariée a montré que parmi les femmes ayant donné naissance à un enfant vivant, celles qui n'avaient suivi qu'une scolarité primaire et qui n'avaient pas regardé la télévision pendant la semaine précédant l'accouchement (facteur utilisé comme indicateur du niveau socio-économique) et celles qui avaient des antécédents de syphilis ou qui avaient eu plus d'un partenaire pendant la grossesse avaient un risque plus élevé de syphilis. Alors que 76 % des femmes participant à l'étude avaient reçu des soins prénatals, seules 17 % avaient fait l'objet d'un dépistage sérologique de la syphilis pendant la grossesse ; 91 % des échantillons de sérum positifs pour le test RPR (test rapide à la réagine) étaient également positifs pour le test FTA-ABS (détection des anticorps spécifiques de tréponème par immunofluorescence indirecte). Les résultats des tests RPR effectués sur les échantillons de sérum dans les laboratoires hospitaliers et les laboratoires nationaux de référence étaient concordants à 96 %. La présence d'une syphilis congénitale a été confirmée par les tests de laboratoire chez 15 % des 66 nourrissons dont la mère avait un RPR et un FTA-ABS positifs.

Conclusion Ces résultats indiquent qu'un programme de prévention de la syphilis congénitale en Bolivie pourrait réduire sensiblement les graves conséquences de cette maladie chez le nourrisson.

Resumen

Sífilis materna y congénita en Bolivia, 1996: prevalencia y factores de riesgo

Objetivo El presente estudio se llevó a cabo en siete maternidades con miras a determinar la prevalencia de sífilis materna en el momento del parto y los factores de riesgo asociados, evaluar un proyecto piloto de prueba rápida para la sífilis en los laboratorios de hospitales, asegurar la calidad de las pruebas de la sífilis, y determinar la tasa de sífilis congénita entre los lactantes nacidos de mujeres con sífilis, todo lo cual había de proporcionar datos basales para un programa nacional de prevención de la enfermedad en Bolivia.

Métodos Se decidió utilizar como muestra de partida para el estudio a todas las mujeres que dieran a luz (incluidos mortinatos) en los siete hospitales participantes, situados en o cerca de La Paz, El Alto y Cochabamba, entre junio y noviembre de 1996.

Resultados Se detectó sífilis en el momento del parto en 61 de 1428 madres (4,3%) de niños nacidos vivos, y en 11 de 43 madres (26%) de mortinatos. El análisis multifactorial reveló que, entre las primeras, presentaban más riesgo de sífilis aquellas que no habían llegado a recibir educación secundaria, que no habían dispuesto de televisión durante la semana anterior al parto (indicador de la situación socioeconómica) y que tenían antecedentes de sífilis o se habían relacionado con más de una pareja durante el embarazo. Si bien un 76% de la población estudiada había recibido atención prenatal, sólo un 17% se había sometido a la prueba de la sífilis durante el embarazo; el 91% de las muestras de suero que dieron positivo en la RPR (prueba rápida de reaginas) también fueron positivas en la prueba FTA-ABS (detección por fluorescencia de anticuerpos anti-treponema absorbidos). Se registró una concordancia del 96% entre los resultados de los laboratorios de los hospitales locales y los laboratorios de referencia nacionales en lo que respecta a la prueba RPR con muestras séricas. La sífilis congénita se vio confirmada por los análisis de laboratorio en un 15% de los 66 niños nacidos de mujeres con resultados positivos en las pruebas RPR y FTA-ABS.

Conclusión Estos resultados indican que la aplicación de un programa de prevención de la sífilis congénita en Bolivia podría reducir sustancialmente los pronósticos negativos por esa causa entre los lactantes.

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