

Is maternal syphilis infection a risk factor for mother-to-child transmission of HIV?

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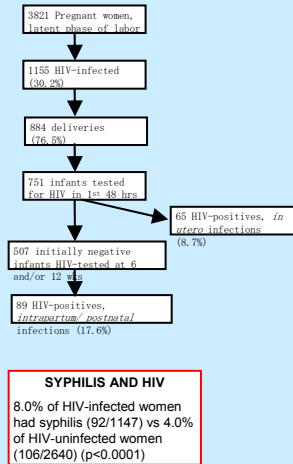
ABSTRACT

Background: HIV and syphilis coinfections are common. We investigated whether maternal syphilis infections in HIV-infected pregnant women are associated with increased risk of Mother-to-Child Transmission (MTCT) of HIV.

Methods: As part of a prospective cohort study investigating the effects of malaria on HIV MTCT, pregnant women admitted at Queen Elizabeth Central Hospital in Malawi were tested for syphilis infection during the latent phase of labor by RPR and confirmed by TPHA. HIV-infected women and their newborn infants received single doses of nevirapine, according to standard protocols. Heel-prick blood samples were collected from infants born to HIV-infected women within 48 hours of birth, and at 6 and 12 weeks postpartum, for HIV-1 detection using HIV DNA PCR. Infants with positive HIV results at birth were classified as being infected *in utero*. Infants with negative results at birth but positive results at 6 and/or 12 weeks postpartum were classified as being infected intrapartum/postnatal.

Results: In univariate analysis, the rate of *in utero* HIV MTCT was higher in syphilis-infected (20.4% [11/54]) than in syphilis-uninfected mothers (7.8% [54/695]); Odds Ratio [OR], 95% Confidence Interval [CI]: 3.04, 1.48–6.23. The rate of intrapartum/postnatal HIV MTCT tended to be higher in syphilis-infected mothers (27.6% [8/29]) than in syphilis-uninfected mothers (17.0% [81/476]), but the difference was not statistically significant (OR, 95% CI: 1.86, 0.80–4.34). In multivariate analysis, maternal syphilis remained significantly associated with *in utero* HIV MTCT even after adjusting for maternal CD4 cell count, maternal fever, birth weight and maternal weight (Adjusted OR, 95% CI: 3.64, 1.52–8.70). Maternal syphilis was also associated with intrapartum/postnatal HIV MTCT in multivariate analysis (Adjusted OR, 95% CI: 3.89 [1.47-10.3]).

Conclusion: These results suggest that maternal syphilis is a risk factor for HIV MTCT. Thus, screening and early treatment of maternal syphilis may reduce pediatric HIV infections, in addition to preventing abortions, stillbirths and congenital syphilis.



STUDY SUBJECTS

Table 1: Characteristic of women who did and those who did not deliver in the study

Characteristic	Delivered in hospital, n (%)	Delivered elsewhere, n (%)	p-value
Median, IQR Age (years)	26 (20.9–28)	21 (26.3)	0.37
Gestational week	38.2 (37.8–38.6)	37.9 (37.5–38.3)	0.04
Primieravidae	25.0% (884)	17.7% (971)	
Secundiaravidae	26.0%	27.9%	
Multiaravidae	49.0%	54.6%	
CD4 (cells/μL) Median	341, 197–515	342, 213–484	0.97
Hb (g/dl) Median, IQR	10.7, 9.4–11.9	10.9, 9.1–11.3	<0.0001
Syphilis infection	434/9 (880)	142/4 (267)	0.09
Peripheral malaria, RPR/TPHA	9.5% (883)	13.0% (269)	0.10
Maternal fever	31.9% (884)	39.0% (269)	0.03
Median, IQR ANC Visits	4.0, 3.0–6.0	3.5, 3.0–5.0	<0.0001
Schooling:			
None	7.8% (884)	12.4% (266)	0.005
Lower Primary School	20.1%	29.0%	
Upper Primary School	39.1%	37.2%	
Secondary or higher	31.9%	21.4%	
Marital Status:			
Single	5.4% (883)	5.4% (883)	0.89
Married	90.3%	90.3%	
Divorced/Separated	4.3%	4.3%	
Housing status:			
Door	1.7% (879)	3.4% (264)	0.09
Fair	22.4%	26.1%	
Good	75.9%	70.5%	

CONCLUSIONS

- Increased maternal HIV RNA viral load was associated with both *in utero* and intrapartum/postnatal MTCT.
- Low birth weight and recent fever were associated with intrapartum/postnatal MTCT
- Placental malaria was not associated with MTCT
- Maternal syphilis was strongly associated with both *in utero* and intrapartum/postnatal transmission
- Better implementation of programs to detect and treat syphilis in pregnant women might reduce MTCT as well as prevent congenital disease

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BACKGROUND

More than 500,000 infants world-wide were HIV-infected perinatally in 2004. This transmission can be partially prevented by nevirapine, and efforts are underway to promote the administration of nevirapine to prevent mother-to-child transmission (MTCT) of HIV.

It is estimated that, in sub-Saharan Africa, approximately 20% of HIV-1 MTCT occur *in utero*, 40-50% *intrapartum* and 30-40% *postnatally*, through breastfeeding.

Infants with detectable virus within 48 hours are considered to have been infected *in utero*. Infants with undetectable virus at delivery, but detectable virus later are considered to be infected either *intrapartum* or *postnatally*

Concurrent infections might promote MTCT by either increasing maternal viral load (such as malaria) or by increasing viral exposure during parturition.

Syphilis infections are common in sub-Saharan Africa. Despite the existence of national programs to test and treat infections during pregnancy, many infections are missed.

METHODS

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Pregnant women, not yet in active labor, were recruited between December 2000 and June 2004 in the antenatal ward of Queen Elizabeth Central Hospital, Blantyre, Malawi.

All women received Voluntary Counselling and Testing for HIV using two rapid tests plus a 3rd tie-breaker. HIV-positive mothers and infants received nevirapine.

Labs: Maternal HIV RNA load, CD4 count, hemoglobin, malaria status (based on placental histopathology), syphilis infection (RPR with TPHA confirmation).

Infant HIV DNA was measured by real-time PCR. Infants positive < 48 hrs of birth were classified as infected *in utero*. Infants negative initially but positive at 6 or 12 weeks were classified as infected intrapartum/postnatally.

Women with recent fever were those with self-reported fever >1 week prior to enrollment, or temperature > 37.5° at enrollment.

RESULTS

Table 2: Univariate predictors in utero and intrapartum/postnatal HIV-1 MTCT

Characteristic	% Infected (n/N)	Odds Ratio (95% CI)	% Infected (n/N)	Odds Ratio (95% CI)
Syphilis Infection			Postnatally	
No	7.8	Reference	17.0	Reference
Yes	20.4 (11/54)	3.04 (1.48 - 6.23)	27.6 (8/29)	1.86 (0.80 - 4.34)
Placental malaria				
No	7.9	Reference	16.3	Reference
Dist. Infection	4.8 (2/56)	1.90 (0.62 - 4.02)	14.0 (2/14)	1.19 (0.60 - 2.40)
Active Infection	11.5 (151)	8.50 (0.99 - 72.1)	15.8 (12/76)	2.40 (0.48 - 12.1)
Low haemoglobin				
Hb count <200	13.1	1.86 (1.02 - 3.37)	13.3	Reference
No	7.8	Reference	14.9	Reference
Yes	4.6 (5/6)	1.92 (0.56 - 6.34)	14.3 (3/58)	1.00 (0.99 - 1.01)
Recent Fever				
No	9.0	Reference	15.1	Reference
Yes	16.7 (179)	1.86 (1.32-2.64)	23.2 (3.29)	1.71 (1.08 - 2.74)
Body Mass Index				
<0.238	8.4	Reference	14.3	Reference
Yes	4.9 (3/7)	1.19 (0.62 - 2.29)	14.8 (4/25)	1.83 (1.02 - 3.29)
Low birth weight				
No	7.9	Reference	15.7	Reference
Yes	14.2 (5/7)	2.86 (1.87 - 4.60)	19.0 (3/17)	2.03 (1.17 - 3.50)
Mode of delivery				
Vaginal	8.7	Reference	18.0	Reference
Elective C-Section	13.0 (12)	1.50 (0.39 - 5.78)	17.6 (4/23)	1.00
Emergency C-Section	4.8 (18)	0.89 (0.47 - 1.69)	18.0 (14/78)	1.00 (0.53 - 1.87)
Sexually Transmitted Infections				
No	8.8	Reference	16.7	Reference
Yes	10.9 (8/23)	1.19 (0.59 - 2.42)	17.4 (4/23)	1.82 (0.75 - 4.51)
Recent Infection				
No	8.8	Reference	16.9	Reference
Yes	10.9 (8/23)	1.19 (0.59 - 2.42)	17.4 (4/23)	1.82 (0.88 - 4.07)
No Antenatal visits				
<4	9.0	Reference	21.0	Reference
>4	4.2 (2/3)	0.66 (0.35 - 1.21)	14.1 (4/28)	0.74 (0.46 - 1.21)

Crude OR's were calculated by simple logistic regression. Variables that were significant at p<0.10 were entered in the multiple logistic regression model as well interaction terms. Any Adjusted OR with a p<0.05 was considered significant.

Table 3: Multivariate predictors of *in utero* and intrapartum/postnatal HIV-1 MTCT

Characteristic	<i>In utero</i> MTCT, OR (95% CI)	p-value	Intrapartum/ postnatal MTCT, OR (95% CI)	p-value
Log10 viral load	1.98 (1.23-3.17)	0.005	2.10 (1.37 - 3.21)	0.000
Recent fever	3.11			0
No	Reference		Reference	
Yes			2.24 (1.23 - 4.10)	0.009
Syphilis infection				
No	Reference		Reference	
Yes	3.64 (1.62- 8.17)	0.004	3.89 (1.47 - 10.3)	0.006
Low birth weight				
No	Reference		Reference	
Yes			2.14 (1.09 - 4.23)	0.03

