MOTHER-TO-CHILD TRANSMISSION OF HUMAN IMMUNODEFICIENCY VIRUS TYPE 1 IN RELATION TO THE SEASON IN YAOUNDE, CAMEROON

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Abstract. A public health program to prevent mother-to-child transmission (MTCT) of human immunodeficiency virus type 1 (HIV-1) by treatment with nevirapine has been ongoing in Yaounde, Cameroon since January 2000. After 24 months, plasma samples from 119 children born to HIV-1-positive mothers were tested for HIV-1 RNA between six and eight weeks after birth. Thirteen (10.9%) tested positive (95% confidence interval = 5.2−16.7%). Risk factors associated with MTCT in this study were maternal viral load (P<0.05), low birth weight (χ² for trend = 8.78, P = 0.01), and birth during the second half of the year. A high correlation was repeatedly observed between rainfall in a given month and the risk of MTCT of HIV-1 in children born three months later (r = 0.634, P < 0.001). Although we cannot rule out other tropical infections related to the rainy season, the role of malaria is highly suspected since the interval of three months we observed between the peaks of rainfall and the rate of transmission is consistent with the Plasmodium life cycle.

INTRODUCTION

In 1997 in Yaounde, Cameroon, the seroprevalence of human immunodeficiency virus (HIV) in a cohort of pregnant women was 4.2%. In 2001, The National AIDS Committee in Cameroon reported an HIV seroprevalence of 11% in pregnant women. Despite the existence of efficient prophylactic interventions to reduce mother-to-child transmission (MTCT) of HIV-1, no intervention was implemented in Cameroon until the year 2000. The main reasons were the costs and complexities of these interventions. However, the HIV-NET 012 clinical trial in Kampala, Uganda that provided single-dose nevirapine to mothers and their children has given new hope to developing countries in their fight against the spread of HIV-1.

Since January 2000, we have implemented a Public Health Pilot Program using nevirapine for the reduction of MTCT of HIV-1 in Yaounde. We performed early diagnosis of HIV-1 infection in infants at 6−8 weeks of age to evaluate the efficacy of this intervention. In this report, we provide information on risk factors associated with MTCT of HIV-1 in our setting, in which the season of birth appeared as the most significant risk factor.

METHODS

Voluntary counseling and testing for HIV were offered to pregnant women during their first visit at an antenatal clinic. Before entering the study, women provided informed consent at the counseling stage. The program was conducted under the auspices of the Cameroon Health Authorities and was reviewed and approved by the Cameroon National Ethical Committee. Women diagnosed as HIV-1 positive were given one dose (200 mg) of nevirapine at the beginning of labor and children were given one dose (2 mg/kg) within the first 72 hours after birth. Formula feeding was recommended, but not provided, in agreement with national health policy. Early diagnosis for HIV-1 infection in children was performed by the detection of viral RNA in plasma samples using a quantification assay (b-DNA technique; Bayer Diagnostics, Paris, France) between six and eight weeks after birth.

Proportions were compared with the Pearson chi-square test, and the dose effect was analyzed by the chi-square test for trend. Means were compared by the analysis of variance or the Kruskal-Wallis test if the variances differed. For logistic regression, the descendant stepwise method was used. All variables were initially introduced with a P value < 0.25. Data collection and analysis were performed using Epi Info software, version 6.04d (Centers for Disease Control and Prevention, Atlanta, GA) with its logistic regression module.

RESULTS

After 24 months, 119 children were tested at the age of 6−8 weeks. Seventeen (14.3%) were breastfed. Among the 119 children tested, 13 (10.9%) were HIV-1 positive (95% confidence interval [CI] = 5.2−16.7%).

Multivariate analysis showed that the risk factors significantly associated with MTCT of HIV-1 in this study were maternal viral load, low birth weight, and birth during the second half of the year. Female sex, which was associated with infection in univariate analysis, was a confounding factor of birth weight in logistic regression. The parity and CD4 cell counts of the pregnant women before delivery were not statistically significant risk factors. Maternal viral load during pregnancy was determined for 52 of the 118 mothers who delivered (one mother delivered twins). Six of the 52 children were infected and 46 were uninfected. There was no MTCT of HIV-1 when the maternal viral load was less than 5,000 copies/mL (Table 1).

The average maternal viral loads values for transmitting and non-transmitting mothers were 185,125 copies/mL (range = 7,157 to > 500,000) and 40,435 copies/mL (range = < 50 to 300,702), respectively (Table 1). The difference in viral loads between the transmitting and non-transmitting mothers was statistically significant (P < 0.05).
The rate of infected children increased when the birth weight decreased: 0% (0 of 29) for children weighing more than 3.5 kg, 9.6% (5 of 52) for those weighing between 3 kg and 3.5 kg, and 23.5% (8 of 34) for those weighing less than 3 kg ($\chi^2$ for trend $= 8.78, P < 0.01$).

Moreover, children born between January and June were less at risk of being infected than those born between July and December: 0% (0 of 51) versus 19.1% (13 of 68); $P < 0.001$.

Pluviometry (rainfall) data were obtained from the provincial delegation for meteorology for the Central Province (Yaounde) of Cameroon. The rate of infected children dramatically increased with the monthly rainfall recorded three months before birth (Table 1). A strong correlation was observed between rainfall in a given month and the rate of infected children born three months later ($r = 0.634, P < 0.001$) (Figure 1). In 2000, the three peaks of rainfall were followed by three peaks of MTCT of HIV-1, and in 2001 the two peaks of rainfall were followed by two peaks of transmission, with the same interval of three months.

Logistic regression (viral load excluded) showed that two variables remained statistically significant: low birth weight (odds ratio [OR] = 5.2, 95% CI = 1.7–16.0) and birth during the second half of the year (OR = 112.2, 95% CI = 4.1–3,103.6).

### DISCUSSION

These data suggest that a pathology related to the rainy season might enhance the risk of MTCT of HIV-1. The interval of three months observed between the peaks of rainfall and the rate of transmission is consistent with the *Plasmodium* life cycle. Furthermore, one of the consequences of malaria infection in pregnant women is the low birth weight of newborns. Moreover, an interaction between placental malaria and HIV infection has been reported. A change in the cytokine profile in malaria-infected placentae, especially an increase in tumor necrosis factor-$\alpha$, could favor HIV-1 replication. These arguments suggest that malaria is the likely pathology related to the rainy season that results in an increase of risk of *in utero* MTCT of HIV-1. Thus, the efficacy of nevirapine in preventing transmission at delivery would be partially obscured in the second half of the year. We are currently conducting prospective studies on malaria parasites within the placenta. However, we cannot rule out the possibility of other factors influencing the transmission rate.

### TABLE 1

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>No. (%)</th>
<th>No. (%) with mother-to-child transmission</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal viral load before delivery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5,000</td>
<td>19 (15.6)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>≥5,000</td>
<td>33 (27.7)</td>
<td>6 (18.2)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>67 (56.7)</td>
<td>7 (10.4)</td>
<td></td>
</tr>
<tr>
<td>Pluviometry (rainfall) data three months before birth (mm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–99</td>
<td>42 (35.3)</td>
<td>1 (2.4)</td>
<td></td>
</tr>
<tr>
<td>100–199</td>
<td>50 (42.0)</td>
<td>6 (12.0)</td>
<td>5.6 (0.6–128.6)</td>
</tr>
<tr>
<td>≥200</td>
<td>27 (22.7)</td>
<td>6 (22.2)</td>
<td>11.7 (1.2–275.8)</td>
</tr>
</tbody>
</table>

*OR = odds ratio; CI = confidence interval.

**FIGURE 1.** Pluviometry (rainfall) data and rate of mother-to-child transmission (MTCT) of human immunodeficiency virus type 1 (HIV-1) in the Yaounde, Cameroon Public Health Program setting over a 24-month period.
bility of another tropical infection related to the rainy season that may also enhance the risk of MTCT of HIV-1. The occurrence of other infections during pregnancy is also being investigated.

In Cameroon, every pregnant woman is given anti-malarial prophylaxis at her first visit to an antenatal clinic. Retrospective studies are ongoing to investigate compliance with chemoprophylaxis. Unfortunately, in Yaoundé, strains of *Plasmodium falcifarum* are highly resistant to several antimalarial drugs that are compatible with pregnancy.5

For obvious reasons of public health, a similar analysis should be performed in areas where malaria is highly endemic to confirm the correlation between the rainy season and the increase risk of MTCT of HIV-1, as well as the potential role of malaria as a risk factor. This observation has already been reported in The Gambia in a cohort of HIV-1-positive pregnant women who had no preventive antiretroviral therapy against MTCT of HIV-1.6

In conclusion, appropriate measures should be taken as soon as possible if our data are confirmed in other areas. We are currently investigating other pathologies affecting pregnant women in our program that could also be related to the rainy season.

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REFERENCES


