

Mother-child transmission of HIV-1 and infant survival in Brazzaville, Congo

Marc Lallemand, Sophie Lallemand-Le-Coeur*, Dominique Cheyner†, Samuel Nzingoula‡, Gonzague Jourdain, Martine Sinet*, Marie-Christine Dazza*, Stéphane Blanche‡, Claude Griscelli‡ and Bernard Larouze*

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The aim of this study was to compare the probability of survival of infants born to anti-HIV-1-positive and anti-HIV-1-negative mothers. One thousand, eight hundred and thirty-three pregnant women, recruited sequentially in two mother-child clinics in Brazzaville, were screened for anti-HIV-1 (by enzyme-linked immunosorbent assay with confirmation by Western blot). Each seropositive mother (71 out of 1833, 3.9%) was matched for age, presumed date of delivery and place of residence with two seronegative mothers. Sixty-four babies born to anti-HIV-1-positive mothers and 130 control babies born to anti-HIV-1-negative mothers were followed up for 12–22 months (mean, 18 months). The probabilities of survival were estimated by the Kaplan–Meier method. At birth, the two groups of babies did not differ with regard to rate of stillbirths, gestational age, sex ratio and weight. Among babies born to seropositive mothers, the probability of survival was 0.87 (s.d. 0.04) at 3 months, 0.71 (s.d. 0.06) at 6 months, 0.68 (s.d. 0.06) at 9 months and 0.61 (s.d. 0.06) at 12.5 months. In the controls the probability of survival was 0.98 (s.d. 0.01) at 3 months and 0.97 (s.d. 0.02) at 12 months. The excess of mortality in the babies born to anti-HIV-1-positive mothers is highly significant ($P < 0.001$). The deaths occurred more frequently and earlier than in similar cohort studies performed in developed countries.

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Introduction

Mother-child transmission of HIV-1 is a major public health problem in central Africa because of the high prevalence rate of HIV-1 infection in young adults (5–20% in urban areas) [1,2] and the high risk (about 30%) of HIV-1 infection in children born to seropositive mothers, as shown by studies performed in European countries [3–5]. In addition, the prognosis of early infection with HIV-1 is especially poor [6].

In Africa, mother-child transmission of HIV-1 may have specific characteristics given the risk factors of maternal

infection and the infectious, nutritional and sociosanitary environments of African children.

A cohort study was therefore designed in Brazzaville, Congo, to evaluate the consequences for infants of maternal seropositivity with emphasis on survival.

Subjects and methods

Between May 1987 and March 1988, 1833 pregnant women were recruited sequentially, after informed consent, at their first prenatal visit to two mother-child clinics serving the

From ORSTOM, Santé/Urbanisation, Brazzaville, Congo, *INSERM U13/IMEA, Hopital Claude Bernard, Paris, France, †Direction de la Santé Maternelle et Infantile, Brazzaville, Congo and ‡INSERM U132, Hôpital Necker-Enfants Malades, Paris, France.

Requests for reprints to: M. Lallemand, ORSTOM, Programme Santé/Urbanisation, 70–74 route d'Aulnay, 93140 Bondy, France.

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eastern districts of Brazzaville, Congo. Women residing outside those districts were excluded. A questionnaire was administered to all of them, which included demographic data, place of residence, socioeconomic status, past obstetric history, as well as record of present pregnancy.

Sera were tested for antibodies to HIV-1 (anti-HIV-1) by enzyme-linked immunosorbent assay (ELISA, ELAVIA; Diagnostics Pasteur, Marnes-La-Coquette, France). ELISA tests were run in duplicate on initially positive sera [differential optical density (DOD) over 0.3] or borderline sera (DOD between 0.2 and 0.3). Confirmation tests of positive results were performed by Western blot (WB) test. Dupont de Nemours, Rockville, USA). Sera were considered positive if they showed antibodies against at least two envelope glycoproteins.

Each seropositive pregnant woman was individually matched for age, presumed date of delivery and place of residence (district) with two seronegative pregnant women. Mothers recruited for the study and their infant(s) were followed up from the birth of the infant (clinical examination and blood sampling) by the same physician at 1 and 3 months and every 3 months thereafter.

The AIDS case definition was that agreed at Bangui (World Health Organization) [7].

Statistical analysis (chi-square tests, two-tailed Fisher exact tests, variance analyses, Kaplan-Meier survival curves [8]) were performed using BMDP statistical software [9]. Statistical significance was designated as $P < 0.05$.

Results

The prevalence rate of anti-HIV-1 in pregnant women was 3.9% (71/1833).

Of the 74 infants (including three pairs of twins) born to anti-HIV-1-positive mothers and their 142 controls, 64 infants and 130 controls were traced and followed up. The others infants were either still-born ($n = 5$, including two born to seropositive mothers) or could not be traced ($n = 17$, including eight born to seropositive mothers) because of changes of residence between the last prenatal visit and the first postnatal visit.

Maternal characteristics of the two groups of live-born infants prospectively followed were compared (Table 1). No significant difference was found for most of the social variables such as occupation, matrimonial status and past obstetric history. Neither did the women differ from the compliance to prenatal follow-up (mean number of prenatal visits and gestational age at first visit). Nevertheless they differed significantly with regard to the number of sexual partners during the year before pregnancy and the duration of relationship, characteristics known as risk factors for HIV-1 infection.

Only one of the seropositive women had AIDS at the time of delivery. After a mean follow-up of 18 months, two additional women had developed AIDS.

The rate of still-birth was similar in the two groups of women: 3% (two out of 66) for seropositive mothers versus 2% (three out of 133) for seronegative mothers.

The comparison of live-born neonates according to the anti-HIV-1 maternal status (Table 2) did not show significant differences for gestational age and sex ratio. Of the

seropositive mothers, 26% delivered a baby weighing less than 2500 g, as compared with 11% of seronegative control mothers ($P < 0.01$). Twins were over-represented among infants born to anti-HIV-1-positive mothers (three pairs of twins versus none). After exclusion of twins, the rates of low birthweights did not differ.

Table 1. Characteristics of mothers according to anti-HIV-1 status

	Anti-HIV-1 positive (n = 64)	Anti-HIV-1 negative (n = 130)	
Occupation (%)*			
Housewife	46	44	
Student	43	46	
Active	11	10	NS
Matrimonial status (%)*			
Single	67	57	
Married	33	43	
Obstetric history			
Mean number of pregnancies	2.2	2.3	NS
Mean parity	1.5	1.8	NS
Primiparous (%)*	36	29	NS
Childhood mortality (%)†	25	16	NS
Pregnancy monitoring			
Mean number of prenatal visits	4.2	4.5	NS
Gestational age at 1st visit (months)	4.3	4.3	NS
Duration of sexual relationship			
1 year or more (%)*	52	35	$P < 0.02$
More than one sexual partner (%)‡	22	7	$P < 0.01$

* % in column; † at least one death of a previously born child; ‡ during the year prior to pregnancy. NS, non-significant.

Table 2. Characteristics of neonates according to maternal anti-HIV-1 status

	Status of mothers		
	Anti-HIV-1 positive (n = 64)	Anti-HIV-1 negative (n = 130)	
Liveborn neonates			
Gestational age of birth < 38 weeks (%)	8	9	NS
Sex ratio (male/female)	1.3	1.2	NS
Twins (%)	9	0	$P < 0.001$
Birth weight < 2500 g (%)	26	11	$P < 0.01$
Birth weight < 2500 g (%) (twins excluded)	18	11	NS
Mean birth weight (g)	2810	3076	$P < 0.01$
Apgar score < 8 (%)	13	12	NS

NS, non-significant.

The survival of infants was analysed after a mean follow-up of 18 months (range, 12–22 months). The analysis of Kaplan-Meier curves (Fig. 1) shows that the probability of survival was significantly lower for children born to seropositive mothers ($P < 0.001$). This probability was 0.98 (s.d. 0.01) at 3 months and remained stable there-

after [0.97 (s.d. 0.02) at 12 months] for children born to seronegative mothers. In contrast, for children born to seropositive mothers, the probability of survival was 0.87 (0.04 s.d.) at 3 months, 0.71 (0.06 s.d.) at 6 months, 0.68 (0.06 s.d.) at 9 months and 0.61 (0.06 s.d.) at 12.5 months.

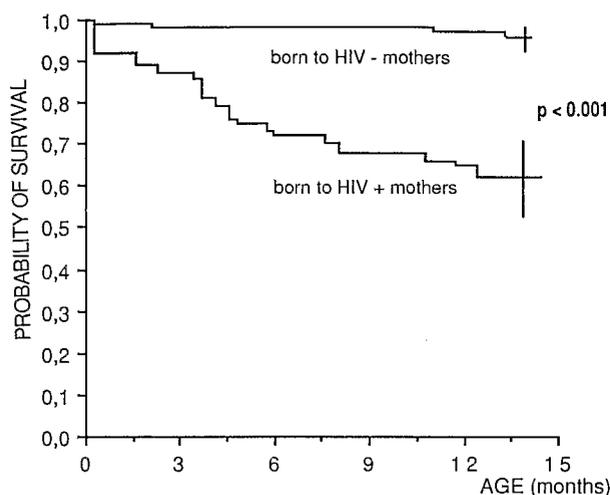


Fig. 1. Survival curves of children born to anti-HIV-1-positive and -negative mothers.

The cause of death among the babies born to anti-HIV-1-negative mothers was related to prematurity (two cases), meningitis (one case) and was unknown in one case. Among the 23 dead babies born to anti-HIV-1-positive mothers, the cause of death was related to prematurity or hypotrophy in five cases (22%), AIDS in eight cases (35%) and acute pulmonary infection and respiratory distress in seven cases (30%). The cause of death could not be assessed in three cases (13%).

Six babies born to seropositive mothers were lost to follow-up during the first year, one during the first, three during the second and two during the third trimesters. Of those babies, four were symptom free and two (6 and 9 months) had clinical symptoms possibly attributable to HIV-1 infection. Of the control babies, 20 were lost for follow-up. All had left Brazzaville for their parents' village.

At the time of the analysis, nine (26%) of the 35 surviving babies born to HIV-1 positive mothers had developed AIDS, eight (23%) had clinical symptoms possibly attributable to HIV-1 infection and 18 (51%) remained symptom free.

Discussion

The prevalence rate for anti-HIV-1 among the pregnant women recruited in the present study ($3.9 \pm 4.5\%$) is similar to that found in a cluster sample survey performed in Brazzaville ($4.6 \pm 2.9\%$; general population 15–45 years old) [1] and among pregnant and parturient women in Kinshasa ($5.8 \pm 0.5\%$), 2 miles away from Brazzaville across the Congo river [10]. These figures confirm the relevance to public health of HIV-1 mother-child transmis-

sion in those capital cities. The problem is even more severe in countries such as Uganda and Rwanda where, in some areas, higher rates of seropositivity have been observed among pregnant women [11,12].

In Occidental studies, no differences were found among newborns according to the anti-HIV-1 maternal status [13] or to the further development of HIV-1 infection [3–5]. In contrast, infants born to seropositive mothers had a significantly lower birth weight and a lower gestational age in a study performed in Kinshasa [10]. In the present study, after exclusion of twins, differences in birth weight according to maternal anti-HIV-1 status followed the same trend but were not significant. This apparent discrepancy might be related to the fact that, in the Brazzaville study, 2% of seropositive mothers (one out of 61) had AIDS versus 18% (85 out of 466) in the Kinshasa study, in which differences at birth were markedly wider when babies born to mothers with AIDS were compared with babies born to seronegative mothers [10].

The greater proportion of twins among infants born to seropositive mothers observed in the present work has not been mentioned in previous reports.

The comparison of children born to seropositive and seronegative mothers, respectively, shows that the high mortality rate in the former group is associated with maternal seropositivity. Seropositive and seronegative mothers are not different in terms of socioeconomic status and parity. Therefore, these variables do not account for the differences in infant mortality rates according to the mother anti-HIV-1 status. Previous cluster sample surveys performed in Brazzaville in 1985 showed infant mortality rates of approximately 6% [14,15]. These rates are higher than among the babies born to seronegative mothers recruited for the present study (3.2%), a finding possibly related to the regular follow-up and improved prevention and medical care, beneficial to those babies and for babies born to seropositive mothers. In the Kinshasa study, the mortality rate among infants born to seronegative mothers was similar (3.8%) [10].

Infant mortality rates among babies born to seropositive mothers were higher in the Brazzaville (39%) and Kinshasa (21%) studies [10] when compared with the European cohort studies (5.5 and 5.8%, respectively, when mortality rates are calculated among infants born to seropositive mothers and not only among infected infants) [3,5]. The difference between the two African studies is possibly because of socioeconomic variables. This is suggested by the variations in mortality rates in Kinshasa (28 versus 16%) according to hospitals receiving women of different socioeconomic status [10].

In this study, in comparison with European studies, the mortality rate was higher and deaths occurred earlier, which may be attributable to differences in environment and in the HIV-1 mother-child transmission rate.

For those African children particularly vulnerable as a consequence of HIV-1 infection, the infectious, parasitic and nutritional context in which they live, may play a major role in the high rate and early incidence of mortality [16]. Even though the children were followed every 3 months, it was difficult to determine the ultimate cause of death for some. Many deaths occurred rapidly and may have been re-

lated to acute bacterial and viral infections. However, the role of environment in central Africa, in comparison with Europe, may not be sufficient to explain the differences in mortality among children born to seropositive mothers; in which case mother-child transmission of HIV-1 rate is higher in Africa.

In the present study, the possible higher transmission rate is not explained by a higher percentage of AIDS cases among seropositive mothers (among seropositive subjects, AIDS cases have been shown to be more contagious [10,17]) as it can be in the Kinshasa study [10]. Heterosexual transmission of HIV-1, the most common cause of seropositivity in African women (as opposed to transmission through intravenous drug use, as in Europe) has not been shown to be associated with a higher HIV-1 mother-child transmission rate [3]. The role of breast-feeding in the mother-child transmission of HIV-1 is strongly suggested by several case reports [18,19] and by the evidence of HIV-1 in the milk of seropositive mothers [20]. The association of breast feeding with HIV-1 mother-child transmission is significant in one [3] out of the three European cohort studies (in fact, these studies included only a small number of nursing mothers) [3,4,5]. In our study, all babies were breast-fed, whereas in European cohorts most are bottle-fed. This should be studied thoroughly since breast-feeding is, at present, a condition of survival for babies in the developing countries. In the absence of easily detectable markers for HIV-1 replication, the role of geographical differences in HIV-1 strains modulating maternal infectivity remains speculative.

The direct evaluation of the HIV-1 mother-child transmission rate was not feasible, since viral isolations were not performed at birth. Furthermore, most deaths occurred during the first year of follow-up and therefore the serological identification of infected infants was not possible because of persistence of maternal antibodies. Even if most children had survived, the long-term latency of HIV-1 infection in some infants might have been responsible for the underestimation of mother-child transmission rates [21]. Therefore, the recently developed application of the polymerase chain reaction technique to the diagnosis of HIV-1 infection might provide accurate figures early in life [22,23], although this technique is still under investigation.

The high prevalence rate of anti-HIV-1 observed in pregnant women and the high mortality in babies born to infected mothers indicate that preventive measures are urgent. At present, prenatal screening for anti-HIV-1 might not be realistic in Africa given the high cost, low feasibility and poor acceptance of subsequent measures (abortion, birth control). The only preventive measures currently implemented in Brazzaville concern sexual and nosocomial (particularly transfusion-related) risk in the general population.

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