

# Retrospective study of maternal HIV-1 and HIV-2 infections and child survival in Abidjan, Côte d'Ivoire

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## Abstract

**Objectives**—To compare the effects of maternal HIV-1 and HIV-2 infections on outcome of pregnancy, infant mortality, and child survival, and to measure serological concordance between mothers and children.

**Design**—Retrospective cohort study with cross sectional study of concordance for HIV antibodies.

**Setting**—Hospital, tuberculosis clinic, and maternal and child health centre in Abidjan, Côte d'Ivoire, west Africa.

**Subjects**—986 women who had had a total of 2758 pregnancies since 1980. The last born children of 194 of these women.

**Main outcome measures**—Pregnancy outcomes; mortality for all children born since 1980; and outcome for last born children. Serological concordance between mothers and last born children.

**Results**—Women with HIV-1 and HIV-2 infections had higher rates of spontaneous abortion and stillbirth than uninfected women (86/769 in HIV-1 positive women, 48/421 in HIV-2 positive, 31/234 in dually reactive, and 96/1131 in uninfected). Compared with children born to uninfected mothers (mortality 10.3%), greater proportions of children of HIV-1 positive (20.6%) and dually reactive (20.3%) mothers had died; mortality in children of HIV-2 infected women (13.1%) was not significantly increased. Infant mortalities for the last born children of HIV-1 positive, dually reactive, HIV-2 positive, and seronegative women were, respectively, 133, 82, 32, and 40 per 1000 live births. Nine of 77 last born children of HIV-1 positive mothers were concordantly seropositive compared with none of 21 children of HIV-2 infected mothers.

**Conclusions**—Maternal HIV-2 infection has less influence on child survival than infection with HIV-1, probably because of a lower vertical transmission rate.

## Introduction

Rates of perinatal transmission of HIV-1 reported from cohort studies range from 13% to 48%.<sup>1</sup> Despite the wide differences in reported transmission rates, which may partly reflect methodological differences, the adverse effect of maternal HIV-1 infection on child survival is unequivocal. The greatest public health impact is seen in countries with high rates of HIV-1 infection in which heterosexual transmission is the main mode of infection. In Zaire,<sup>2</sup> the Congo,<sup>3</sup> and Haiti,<sup>4</sup> for example, the probabilities of children of HIV-1 infected mothers dying in the first year of life were 21%, 29%, and 23% respectively, significantly higher than the rates in children of uninfected women.

Vertical transmission of HIV-2, and the impact of maternal HIV-2 infection on child health, have been little studied.<sup>5,6</sup> Although vertical transmission of HIV-2 has been shown,<sup>7,9</sup> cross sectional studies in west Africa examining mothers infected with HIV-2 and their children suggest that this is rare.<sup>10-13</sup> The limited information available from prospective studies

supports this conclusion (T S Sibailly *et al*, eighth international conference on AIDS and third sexually transmitted disease world congress, Amsterdam, July 1992; Abstract WeC 1065).<sup>13</sup>

To gain insight into the comparative effects of maternal HIV-1 and HIV-2 infections on child survival we compared obstetric histories and reported child mortality, as well as serological concordance with children, of women with HIV-1 and HIV-2 infections in Abidjan, Côte d'Ivoire, west Africa.

## Subjects and methods

We invited women identified through other research activities as testing positive for HIV-1 or HIV-2, or both, as well as seronegative women to participate. Diagnosis of HIV-1 and HIV-2 infections was based on results of whole virus enzyme linked immunosorbent assay and western blot, or synthetic peptide tests, or both.<sup>14,15</sup> We recruited women from three sites: a maternal and child health centre where women attended for child birth, a hospital ward where most of the women recruited were visiting their spouses, and a tuberculosis treatment centre where women were attending for care.

A standard questionnaire was administered about the women's obstetric histories since 1980. The questions included the numbers of pregnancies, their outcome (live birth, stillbirth, or spontaneous or induced abortion), and whether liveborn children were still alive. For children who had died, the date of death or age at death was recorded. When possible, living children aged 1-9 years at the time of the study were tested for HIV-1 and HIV-2 antibodies.

We analysed data using statistical software packages for epidemiological analyses, including SAS and EPI INFO. Obstetric outcomes and reported child deaths in women of different serostatus were compared in a retrospective cohort analysis; we calculated relative risks and 95% confidence intervals and constructed Kaplan-Meier survival curves. Maternal serological concordance with children was compared between women of different serostatus using Fisher's exact test. Alpha was set at 0.05. The study received ethical approval from the Côte d'Ivoire national AIDS committee.

## Results

Of the 986 women who participated in the study, 529 were recruited from the maternal and child health centre, 396 from the hospital, and 61 from the tuberculosis treatment centre. With the exception of the women in the tuberculosis treatment centre, most of the HIV positive women were asymptomatic. The centres used for recruitment provide services for the indigent population of Abidjan, and the women were of low socioeconomic status. Table I shows the characteristics of the 986 women studied. Mean age and parity were similar in all serological groups.

Table II shows the outcome of pregnancies since 1980. After induced abortions were excluded from the

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analysis, 11.1% (86/769) of pregnancies in HIV-1 positive women ended in spontaneous abortion or stillbirth compared with 8.5% (96/1131) of pregnancies in seronegative women (relative risk 1.3, 95% confidence interval 1.0 to 1.7). The respective rates for HIV-2 positive and dually positive women were 11.4% (48/421; 1.3, 0.97 to 1.9), and 13.2% (31/234; 1.6, 1.1 to 2.3).

Children born alive to HIV-1 positive or dually reactive women since 1980 were significantly more likely to have died than children of seronegative women. Of liveborn children born to HIV-1 positive mothers, 20.6% (140/681) with known outcome had died, compared with 10.3% (106/1034) of children of seronegative mothers (2.0, 1.6 to 2.5). Total mortality for liveborn children of dually positive women was 20.3% (41/202); (2.0, 1.8 to 2.8). The proportion of children of HIV-2 positive women who had died was 13.1% (49/373), not significantly different from that in children of seronegative women (1.3, 0.9 to 1.8). Figure 1 shows the Kaplan-Meier survival curves for children of mothers of different serostatus.

Differences in survival were particularly obvious when outcome of only the last pregnancy was considered: 6% (23/354) of those born to seronegative women had died compared with 24% (58/240) born to HIV-1 positive women (3.7, 2.4 to 5.9) and 22% (19/85) born to dually reactive women (3.4, 2.0 to 6.0). The proportion of last born children of HIV-2 positive mothers who had died was 6% (8/126), similar to the rate for children of uninfected mothers.

Figure 2 shows the Kaplan-Meier survival curves for the last born children. Infant mortality (deaths in the first year of life per 1000 live births) for last born children of HIV-1 and dually reactive mothers were 133/1000 and 82/1000 respectively, compared with 32/1000 and 40/1000 for HIV-2 infected and seronegative women.

Table III shows the serological concordance between 194 mothers and their last born children. The concordance rate for children of HIV-1 positive mothers

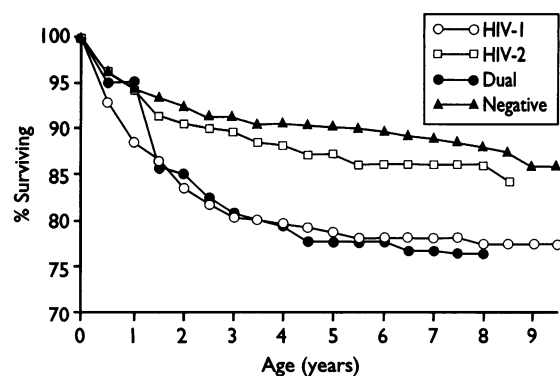


FIG 1—Survival of children born since 1980 according to HIV serostatus of mothers. (Curve truncated when less than 20 children remained)

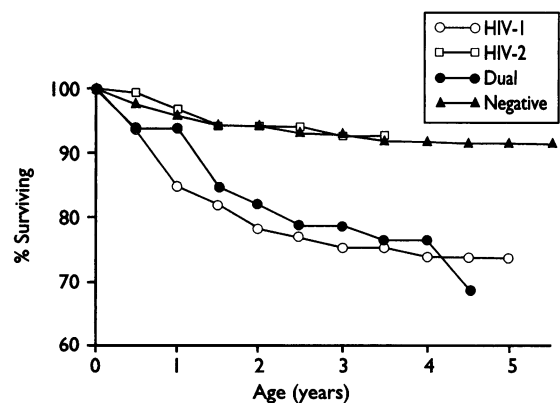


FIG 2—Survival of last born children according to HIV serostatus of mothers. (Curve truncated when less than 20 children remained)

was 12% (9/77). In contrast, none of 21 children of HIV-2 positive mothers was infected with HIV-2 ( $P=0.2$ ). Of children of dually reactive mothers, 11% (2/18) were HIV-1 positive and 6% (1/18) HIV-2 positive. Discordant positive results were found in one child of a HIV-2 positive mother and two children of seronegative mothers. These discordant infections are presumed to have come from another source.

## Discussion

Adverse obstetric outcome, including spontaneous abortion and stillbirth, has been found to be associated with maternal HIV-1 infection in Africa.<sup>16-18</sup> Women in Abidjan with HIV-2 infection or with dual serological reactivity also reported an increased rate of stillbirth and spontaneous abortion. A prospective study of the influence of HIV-1 and HIV-2 on obstetric outcome is needed which takes into account the role of other sexually transmitted diseases.

In this retrospective study, children of HIV-2 infected mothers in Abidjan had similar survival to children of seronegative women, in contrast to the increased overall mortality in children of HIV-1 positive mothers. Infant mortality for the last born children of HIV-1 infected mothers was more than four times higher than for children of HIV-2 positive women (133/1000 *v* 32/1000, respectively).

Although HIV-2 can be transmitted perinatally, the frequency of transmission is uncertain. Results from a prospective cohort study in Abidjan (T S Sibailly *et al*, eighth international conference on AIDS and third sexually transmitted diseases world congress, Amsterdam, July 1992; Abstract WeC 1065) showed mother to child transmission of HIV-2 to be at least 20 times less common than that of HIV-1. In keeping with the results of studies in Guinea Bissau<sup>10</sup> and the Gambia,<sup>11</sup> we found serological concordance rates between mothers and their living children in Abidjan to be

TABLE I—Characteristics of women studied according to serological status

	HIV-1 (n=306)	HIV-2 (n=156)	HIV-1 and HIV-2 (n=102)	No infection (n=422)	Total (n=986)
Total pregnancies since 1980	841	450	246	1221	2758
Mean pregnancies since 1980	2.7	2.8	2.4	2.9	2.8
Mean lifetime pregnancies	3.8	3.6	2.9	4.0	3.8
Mean (range) age (years)	27.5 (13-52)	27.8 (19-42)	27.5 (18-44)	28.5 (14-51)	28.0 (13-52)

TABLE II—Outcome of pregnancies since 1980 in women stratified by serological status. Data are numbers (percentages)

Outcome	Maternal HIV status				Total
	HIV-1	HIV-2	HIV-1 and HIV-2	None	
Stillbirth	25 (3.0)	15 (3.3)	11 (4.5)	26 (2.1)	77 (2.8)
Spontaneous abortion	61 (7.3)	33 (7.3)	20 (8.2)	70 (5.7)	184 (6.7)
Induced abortion	72 (8.6)	29 (6.4)	12 (4.9)	90 (7.4)	203 (7.4)
Live born, child died	140 (16.7)	49 (10.9)	41 (16.7)	106 (8.7)	336 (17.2)
Live born, child living	541 (64.5)	324 (72.0)	161 (65.7)	928 (76.1)	1954 (71.0)
Total	839	450	245	1220	2754

Outcome unknown for two liveborn children of HIV-1 positive mothers, one child of dually reactive mothers, and one child of seronegative mothers.

TABLE III—Serological concordance for HIV-1 and HIV-2 antibodies between mothers and their 1-9 year old last born children

Maternal serological status	Children's serological status				Total
	HIV-1	HIV-2	HIV-1 and HIV-2	None	
HIV-1	9	0	0	68	77
HIV-2	1	0	0	20	21
HIV-1 and HIV-2	2	1	0	15	18
None	1	0	1	76	78
Total	13	1	1	179	194

### Public health implications

- The rate of mother to child transmission of HIV-2 is believed to be considerably lower than that of HIV-1
- In this study survival of children born to HIV-1 and dually reactive women was greatly reduced compared with that for children of seronegative and HIV-2 positive women
- Nine of 77 children of HIV-1 positive mothers but none of the 21 children of HIV-2 positive mothers were concordantly seropositive
- Perinatal transmission of HIV-2 is much less efficient than that of HIV-1, resulting in more favourable child survival

lower for HIV-2 than for HIV-1, consistent with a lower probability of perinatal HIV-2 transmission.

Increased survival of children of HIV-2 positive mothers could theoretically result from a different natural course of HIV-2 infection in children, with slow progression to AIDS. Despite the apparent differences in the natural course of HIV-1 and HIV-2 infections in adults (T Siby, *et al*, eighth international conference on AIDS and third sexually transmitted diseases world congress, Amsterdam, July 1992; Abstract WeC 1066) there is no doubt that HIV-2 infection is associated with clinical immune deficiency<sup>5 6 14</sup> and increased mortality.<sup>19 20</sup> It is unlikely that HIV-2 infection would be entirely benign in children. The evidence suggests that the more favourable survival of children of HIV-2 infected mothers results from the very low rate of HIV-2 mother to child transmission.

A potential confounding factor in this study is duration of maternal HIV-1 and HIV-2 infections since advanced immunodeficiency is a known risk factor for perinatal transmission and therefore adverse child survival.<sup>21</sup> It is uncertain when HIV-1 and HIV-2 were introduced into Abidjan,<sup>5 6</sup> and the time of acquisition of maternal HIV-1 and HIV-2 infections in this study is unknown. The epidemic of AIDS is recent,<sup>19</sup> however, and HIV-2 is likely to have been present at least as long as HIV-1.<sup>5</sup> Mean age and parity were similar across the different serological groups, suggesting duration of infection with these sexually transmitted agents should be broadly similar in the different groups. It is possible, however, that HIV-2 infection is often acquired at an older age than HIV-1,<sup>21a</sup> and conclusions about duration of infection should not be drawn from cross sectional data.

We evaluated the outcome of pregnancies and live births since 1980 to ensure that all pregnancies and infants potentially affected by maternal HIV-1 or HIV-2 infection would be included. In addition, we examined the outcome of last born children only, because these children would have been the most likely to have been born when the mother was already infected. Conclusions from analyses of all births since 1980 and of lastborn children only were similar.

Dual reactivity to HIV-1 and HIV-2 is poorly understood.<sup>22</sup> Survival of children born to dually reactive mothers was similar to that of children of HIV-1 infected mothers. Of the three seropositive children of dually reactive mothers, two were HIV-1 positive and one HIV-2 positive. The proportion of dually reactive women who are genuinely infected with both HIV-1 and HIV-2 is uncertain,<sup>22</sup> but molecular studies indicate that between one third and two thirds of dually reactive people in Abidjan are infected with both viruses and that most of the others are infected with HIV-1.<sup>23 24</sup> Survival of children of dually reactive

mothers is similar to that for children of HIV-1 infected mothers, suggesting that dually reactive mothers transmit HIV-1 infection in a substantial proportion of cases.

Based on the more favourable survival of children of HIV-2 positive mothers, as well as current knowledge of mother to child transmission of HIV-2, public health advice concerning the risk of perinatal transmission of HIV-2 should be modified to reflect these epidemiological differences between HIV-1 and HIV-2 infections.

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