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ORIGINAL ARTICLE

HIV-1 infection and reproductive history: a retrospective study among pregnant women, Abidjan, Côte d'Ivoire, 1995–1996

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Summary: The aim of this paper is to determine the differences of fertility between HIV-1 infected and uninfected women in Abidjan, Côte d'Ivoire, using data available in an observational study conducted in 1995 and 1996 in 2 antenatal care centres in the district of Yopougon, Abidjan, within an intervention programme to reduce mother-to-child HIV-1 transmission (DITRAME project, ANRS 049).

Fertility indicators have been constructed from retrospective data on pregnancies and births, and univariate and multivariate analyses have been performed on these indicators and stratified by age groups to compare HIV-1 positive and HIV-negative populations. The main outcome measures were the number of pregnancies, the number of miscarriages, the risk of miscarriage and the proportion of primigravida. Four thousand, three hundred and ninety-six women agreed to HIV testing: 12.1% were found to be HIV-1 infected. HIV-1 positive women had significantly fewer pregnancies than HIV-negatives in age-groups 25–29 (P=0.05) and 30–34 (P=0.008). The risk of having had at least one abortion or stillbirth was significantly higher for HIV-1 infected women than for HIV-negatives (OR=1.28, 95% CI: 1.02–1.60), when controlling for social and demographic factors. This study suggests that HIV-1 infection has deleterious consequences on female fertility, with lower fertility rates and more frequent adverse pregnancy outcomes. Family planning and antenatal care services should consider antenatal HIV counselling and testing in women in areas of high HIV prevalence.

Keywords: HIV-1 infection, fertility, pregnancy, miscarriage, abortion, stillbirth

INTRODUCTION

The HIV epidemic is thought to have important effects on fertility and reproductive decisions in African countries, where there is a high prevalence of HIV in women of reproductive age. Yet, little is known about the association between HIV infection and fertility, which is itself the result of biological, epidemiological and cultural factors.

It has been postulated that men and women infected by HIV who become aware of their serostatus may be prompted to have children sooner. This attitude could have important short-term consequences for perinatally-infected infants and in the longer term uninfected children may be more likely to become orphans[1]. Access to social support in most African settings is linked to decision of HIV-positive individuals to become parents[2]. HIV awareness however may not substantially influence choices about reproduction, as few African women know their HIV-serostatus and those who become aware generally do so owing to symptomatic HIV disease, at a time when their overall fertility can no longer be modified. African studies have shown that HIV-positive persons who become aware of their status are reluctant to tell their partners, even after intensive counselling[3–5]. In the African context, women are unlikely to negotiate safer sex or reproductive choice with men and contraception remains an uncommon practice[2]. Therefore, the consequences of the HIV epidemic on fertility in Africa can be investigated more using demographic data than through behavioural

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changes. First, the most fertile age groups are those of greater risk of infection and death[6]. Secondly, studies in Africa and Europe have shown significant associations between HIV infection and lower fertility rates or greater primary infertility[7–9]. At an individual level, HIV may damage the reproductive physiology, in synergy with other STDs. HIV-positive women are known to have poor outcomes of pregnancy[10].

The aim of this study is to analyse and compare information on pregnancy and births collected among HIV-1 infected and uninfected pregnant women attending a voluntary counselling and testing centre in the context of an intervention programme to decrease mother-to-child transmission of HIV-1, the DITRAME project (ANRS 049), in order to evaluate whether there were any differences in fertility.

METHODS

In February 1995, a research intervention programme to reduce mother-to-child transmission of HIV (Essai DITRAME ANRS 049) commenced in a community health centre, the Formation Sanitaire Urbaine (FSU) of Yopougon, located in one of the urban districts of Abidjan, the largest city of Côte d'Ivoire, West Africa.

The first step of this programme was to implement HIV voluntary counselling and testing among pregnant women susceptible to be offered enrolment into a clinical trial of zidovudine (AZT) to prevent mother-to-child transmission of HIV[11–13]. HIV testing was offered, after pre-test counselling, to those who fulfilled the following criteria: aged 18 years or more, planning to deliver in Abidjan and pregnancy under 32 weeks. After written consent was given, a blood sample was tested for HIV and syphilis serology. HIV-infected women were offered entry to the therapeutic trial during the post-test counselling visit.

We considered only HIV-1 infection in this study. Obstetric data about the total number of pregnancies, abortions, stillbirths and live births were collected during the pre-test interview. No further information on birth dates or intervals were available. Induced or spontaneous abortions were not distinguished. Fertility indicators were constructed using these data. Univariate analyses were performed by age group to compare the HIV-1 infected and the HIV-uninfected groups on the following criteria: the mean number of pregnancies, the proportion of primigravida, the mean number of abortions or stillbirths and the proportion of women having had at least one abortion or stillbirth. The first 2 indicators give information on the ability of a woman to become pregnant. The last 2 give information on the risk of adverse pregnancy outcomes.

Multivariate logistic regression was then used to model the risk of having had at least one abortion or one stillbirth in the presence of HIV-1 infection while controlling for possible confounding factors: age, marital status, number of pregnancies, religion and level of instruction. These factors were included because they were significantly related to the fertility indicators in univariate analysis, and because previous studies in our population have identified a relationship with HIV infection[14].

For both the univariate and multivariate analyses of abortion or stillbirth, primigravida have been excluded since they could not have experienced such an event.

RESULTS

During the 2-year study period, 4396 women were tested for HIV. Five hundred and two (11.4%) were found to be HIV-1 positive, 60 (1.4%) were HIV-2 positive, and 29 (0.7%) were infected both by HIV-1 and HIV-2. The 60 women infected only by HIV-2 were excluded from the analysis, and 35 women whose age was not known were also excluded. Among the 4301 women left, 12.3% were HIV-1 infected (501 HIV-1+ and 29 HIV-1+ and HIV-2+).

Relationship between HIV-1 infection and the ability to become pregnant

The mean number of pregnancies was higher in the HIV-1 positive group than in the HIV-negative group for women less than 20 (P=0.005, Table 1). Conversely, in the age range 25 to 34, HIV-1 positive women have had fewer pregnancies than HIV-negatives, these differences being again statistically significant (Table 1). The proportion of primigravida was approximately the same in both groups (Table 1).

Table 1. Mean number of pregnancies and proportion of primigravida by age and HIV-1 status (Ditrame Project, Abidjan, Côte d'Ivoire, 1995–1996, n=4301*)*

Age group (years)	Mean number of pregnancies			Proportion of primigravida (%)			Nb. of women
	HIV-1+	HIV−	*P* value*	HIV-1+	HIV−	*P* value**	
<20	2.0	1.7	0.005	39	51	0.05	653
20–24	2.5	2.6	0.61	18	20	0.47	1484
25–29	3.6	3.9	0.05	7	5	0.39	1079
30–34	4.7	5.4	0.008	5	2	0.19	739
⩾35	7.2	7.2	0.94	4	0	0.02	346

*Student's *t*-test, **Chi-square test

Relationship between HIV-1 infection and abortion or stillbirth

In univariate analysis, HIV-1 infection appears to be related to an increase of abortion or stillbirths, but differences are significant only for some age groups, and mainly for stillbirths. In the 25–29 age group, the mean number of stillbirths in the HIV-1 positive group was 0.19 against 0.08 in the HIV-negative group (Student's *t*-test, P=0.002); 14% of the HIV-1 seropositive women aged 25–29 had already had a stillbirth against 7% of the HIV-1 negative from the same group of age (χ^2 test, P=0.01). No other statistical difference was observed in terms of proportion in the comparison performed by age group although the tendency was in favour of a higher risk of miscarriage for HIV-1+ women at the age of 35 or above (Figure 1).

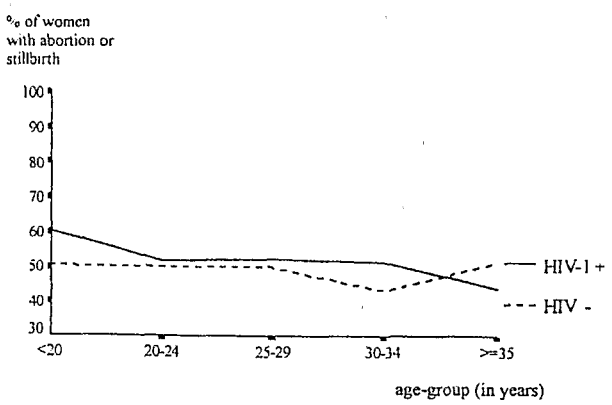

Figure 1. Proportion of women having had at least one abortion and/or stillbirth by age and serostatus. Ditrame Project, Abidjan, Côte d'Ivoire, 1995–1996 (primigravida excluded, n=3611)

In multivariate analysis, the association between HIV-1 infection and abortion or stillbirth becomes significant when controlling for factors strongly related to fertility such as age, marital status, number of pregnancies, religion and level of instruction. Table 2 shows that the adjusted odds ratio of having had at least one abortion or stillbirth is 1.28 (95% CI: 1.02–1.60) between HIV-1 infected and HIV-1 uninfected women. For at least one stillbirth, the adjusted odds ratio is 1.52 (95% CI: 1.04–2.21). For at least one abortion, the adjusted odds ratio is 1.15 (95% CI: 0.92–1.44).

The overall risk of abortion or stillbirth is related to each of the factors studied, but the risk of abortion and the risk of stillbirth show different patterns. The risk of abortion appears strongly related to the 5 factors studied. It is greater for the younger women than for women older than 30 (Table 2). The risk of abortion is lower when the woman is not single or when she declares Muslim religion (OR=0.48, 95% CI: 0.38–0.60) and (OR=0.75, 95% CI: 0.61–0.92), respectively (Table 2). At the same time, we observe that this risk increases with the level of instruction (Table 2).

On the other hand, the risk of having had a stillbirth is not related to the abovementioned sociodemographic factors. It depends only on the number of pregnancies (the risk of stillbirth is

Table 2. Multiple logistic regression analysis of the risk of having had at least one abortion or stillbirth. Ditrame Project, Abidjan, Côte d'Ivoire, 1995–1996 (primigravida are excluded from the analysis, n=3611)

	Risk of having had		
	At least one abortion or stillbirth	At least one abortion	At least one stillbirth
Variable	Odds ratio (95% CI*)	Odds ratio (95% CI*)	Odds ratio (95% CI*)
Age-group			
<20	3.94 (2.63–5.90)	4.23 (2.82–6.37)	1.20 (0.59–2.47)
20–24	3.15 (2.25–4.40)	3.56 (2.54–4.99)	0.96 (0.57–1.60)
25–29	1.98 (1.45–2.71)	2.18 (1.59–2.99)	0.94 (0.59–1.50)
30–34	0.99 (0.74–1.34)	1.14 (0.85–1.55)	0.73 (0.47–1.14)
⩾35	ref.	ref.	ref.
Marital status			
Marital/non marital	0.50 (0.40–0.63)	0.48 (0.38–0.60)	1.36 (0.85–2.19)
Number of pregnancies			
2–3	0.12 (0.09–0.17)	0.13 (0.10–0.18)	0.19 (0.15–0.31)
4–6	0.41 (0.32–0.54)	0.40 (0.31–0.52)	0.59 (0.40–0.86)
⩾7	ref.	ref.	ref.
Religion			
Muslim	0.80 (0.11–0.97)	0.75 (0.61–0.92)	1.12 (0.78-1.60)
Christian	1.29 (1.08–1.54)	1.30 (1.08–1.55)	1.00 (0.73–1.39)
Others	ref.	ref.	ref.
Level of instruction			
None	0.23 (0.19–0.28)	0.23 (0.19–0.27)	0.78 (0.55–1.11)
Primary	0.45 (0.37–0.54)	0.42 (0.35–0.50)	1.07 (0.76–1.49)
Secondary	ref.	ref.	ref.
HIV status			
HIV-1+/HIV−	1.28 (1.02–1.60)	1.15 (0.92–1.44)	1.52 (1.04–2.20)

*95% confidence interval of the odds ratio

smaller for women with 3 pregnancies or less) and on HIV-1 status (Table 2).

DISCUSSION

Our data suggest important differences in fertility between HIV-1 positive and HIV-negative women, especially for certain age groups, however it must be borne in mind that the data analysed here were not collected on the purpose of studying fertility. The aim of this study was to analyse data collected during the intervention programme in order to throw light upon interactions between HIV infection and fertility, a subject about which little is known. Hence some important information is lacking, in particular reference to possible co-infection of the pregnant woman with STDs, and the distinction between spontaneous and induced abortion. Moreover, these data are retrospective. Therefore the duration of HIV infection is unknown. Despite these limitations, the analysis reveals significant trends. Since relationships with fertility have been previously described only for HIV-1[7,9,15] and since HIV-2 is not thought to have consequences on women's fertility, we only considered HIV-1 infection in this study. Behavioural differences may account for the larger mean number of pregnancies found in the HIV-1 infected group for the youngest age category: HIV-1 infected young women are postulated to have more sexual contacts than HIV-1 uninfected ones and therefore are more likely to become pregnant, since contraception is not commonly used in this population. In 1996, in the Yopougon district, only 6% of the women aged 15–19 were using a modern contraception method[16]. Alternatively, the smaller mean number of pregnancies found in the HIV-1 positive group for women aged 25 to 34 cannot be completely explained by behavioural differences. Knowledge of HIV positivity cannot have influenced a change in sexual behaviour, since the women were unaware of their HIV status at the time of the interview. Indeed, these HIV-1 positive women might have reduced their sexual activity, if either they or their partners became ill. However this population of women were asymptomatic from HIV-1. Thus, it seems more likely that the lower number of pregnancies observed in the HIV-1 positive group suggest a poorer physiological ability to become pregnant. Further information on contraceptive use and on sexual relations are necessary to confirm this hypothesis.

The main difficulty in explaining the observed relationship between the risk of negative pregnancy outcomes and HIV-1 infection is the possible heterogeneity of these cases: it is not always possible to distinguish abortion and stillbirth; an abortion is registered when the mother declares a pregnancy lasting less than 6 months, and it is considered as a stillbirth when the pregnancy lasts more. Since the duration of the pregnancy is estimated only by the mother's report, the 6 months time limit is imprecise. Secondly, abortion can be induced or spontaneous; in the first case it is a behavioural pattern, in the second case a biological fact. We have suggested why HIV infection is not expected to have changed women's behaviour, since at the time of interview, women were unaware of their HIV status. Therefore, the independent effect of HIV-1 infection on the risk of abortion observed in our multivariate analysis suggests that HIV-1 infection would have consequences on female fertility, by increasing the biological risk of miscarriage during pregnancy.

From our data, this effect seems to concern stillbirths more than abortions. But the biological effect of HIV infection on spontaneous abortion may be partly hidden by the induced abortion phenomenon: the strong relationships observed in our analysis between the risk of abortion and religion, marital status, level of instruction suggest the importance of induced abortion in the total number of abortion events. Therefore, HIV-1 infection may increase the risk of spontaneous abortion more than seen here, as well as increasing the risk of stillbirth.

Consequences of associations between HIV and female fertility are important, since these effects may combine with other social and epidemiological factors that influence both fertility and risk of HIV infection. For HIV-positive African women who are trying to get pregnant, higher rates of miscarriages and higher neonatal and infant mortality will shorten periods of post-partum abstinence usually respected, with consequences on the woman's health and fertility and on the risk of infection of her partner if he is not already infected himself. Therefore there is an urgent need for a better knowledge of these complex associations between HIV, fertility and STDs, which should be taken into account in all health reproductive programmes[17] like AIDS prevention programmes, family planning programmes, AIDS counselling programmes, maternal and child health care, etc. Furthermore, this hypothesis of a difference in the fertility of HIV-infected and HIV non-infected women needs to be verified, on one hand for its demographic and health consequences and on the other, since in many countries, estimates of HIV prevalence are performed from unlinked anonymous prevalence studies among pregnant women which are often viewed as a rough estimate for prevalence in all women of childbearing age.

CONCLUSION

The data on fertility collected in the context of the Ditrame project show a significant association between HIV-1 infection and lower fertility, even if they were not collected for this purpose and thus were not suitable to make a complete analysis of such a relationship. These data suggest that HIV-1 infection increases the risk of abortion and even more the risk of stillbirths. Nevertheless, these

results must be considered as preliminary and call for more investigation: another survey is underway in the same population of pregnant women, in order to collect data on induced and spontaneous abortions, on contraception as well as on age at first birth. Thus specific studies must be conducted, in order to have a better knowledge of the relationship between HIV infection and fertility and to better understand the characteristics of HIV-infected women fertility. This knowledge is of first importance in order to adapt family planning as well as maternal and child health-care programmes to a population where 12% of the pregnant women are infected by HIV-1.

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