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THE ASSOCIATION BETWEEN HIV AND FERTILITY IN A COHORT STUDY IN RURAL TANZANIA

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Summary. Recent studies in sub-Saharan Africa have shown that fertility is reduced among HIV-infected women compared with uninfected women. The size and pattern of this fertility reduction has important implications for antenatal clinic-based surveillance of the epidemic and also for estimates and projections of the demographic impact of the epidemic. This paper examines the association between HIV and fertility in Kisesa, a rural area in Tanzania, where HIV prevalence among adults is about 6% and gradually increasing. The analysis is based on data obtained through a demographic surveillance system in Kisesa during 1994–98 and two large sero-surveys of all residents in 1994–95 and 1996–97. The HIV-associated fertility reduction among women was investigated by estimating fertility rates by HIV status and prevalence rates by fertility status. A substantial reduction (29%) was observed in fertility among HIV-infected women compared with HIV-uninfected women. The fertility reduction was most pronounced during the terminal stages of infection, but no clear association with duration of infection was observed. Use of modern contraception was higher among HIV-infected women. However, both among contracepting and non-contracepting women, a substantial reduction in fertility was seen among HIV-infected women.

Introduction

A growing body of evidence now exists to support the hypothesis of reduced fertility among HIV-infected women relative to their HIV-uninfected peers. Cohort studies in rural Uganda and urban Zaire have shown significant and fairly consistent fertility reductions among HIV-infected women. In Rakai, Uganda, the relative risk of an infected woman giving birth was 0·8 relative to an uninfected woman

(Sewankambo *et al.*, 1994). In Masaka, Uganda, the overall age-adjusted fertility rate in HIV-infected women was 0.74 times that of uninfected women (Carpenter *et al.*, 1997). In Kinshasa, Zaire, the fertility rate ratio in a cohort of women recruited from hospital following the delivery of a child was 0.77, adjusted for contraceptive use (Ryder *et al.*, 1991).

A difference in fertility rates between HIV-infected and uninfected women has implications for the measurement of HIV prevalence in populations. A search of the US Bureau of the Census, HIV/AIDS surveillance database, showed that over 60% of studies estimating HIV prevalence in the developing world are based on blood samples taken from antenatal women (US Bureau of the Census, 1998). If fertility differentials by HIV status are not taken into consideration when interpreting HIV prevalence estimates from sentinel surveillance of antenatal clinic attendees, serious underestimates could be made of the total number of women infected. Fertility differentials by HIV status also have implications for orphanhood estimates and projections, as well as for the cost of mother-to-child transmission reduction programmes.

HIV is known to have a direct impact on fertility due to biological factors including increased risk of spontaneous abortions and stillbirths (Miotti *et al.*, 1990; Brocklehurst & French, 1998). In the later stages of the disease there is increased amenorrhoea (Widy-Wirski *et al.*, 1988). In men, it reduces spermatogenesis (Krieger *et al.*, 1991), and lower coital frequencies have been reported by couples in which the male partner has begun to suffer from opportunistic infections (Dublin *et al.*, 1993).

Behavioural responses to the epidemic may alter fertility in the whole population, although they are likely to affect HIV-positive women more than the HIV-negative, contributing to observed fertility differentials. Studies in Uganda and Zimbabwe indicated higher rates of widowhood, higher divorce rates as a result of knowledge or suspicion of HIV infection in either partner, and lower re-marriage rates (Muzika-Gapere & Ntozi, 1996; Gregson *et al.*, 1997). A study in Zaire (Ryder *et al.*, 1991) noted higher rates of postpartum contraceptive use among HIV-positive women. On the other hand, it has been suggested that some behavioural changes may cause increases in fertility. For example, in Zimbabwe, decreases in breast-feeding have been reported amongst women who know that the virus may be transmitted to infants through breast milk (Gregson *et al.*, 1997).

Although infection with HIV is generally thought to cause lower fertility, it is also possible that reverse causation and selection effects contribute to the observed relationship. Many African societies place great importance on bearing children, putting great pressure on women who experience difficulty in having children. A study in Uganda (Ross *et al.*, 1999) found that pre-existing differences in the gravidity of women accounted for almost half of the observed differences in the fertility of HIV-infected and uninfected women. A study in Gabon showed age-adjusted HIV prevalence to be far higher among women with primary infertility than among fertile women (Schrijvers *et al.*, 1991). In Tanzania, HIV prevalence was markedly higher among infertile women than among fertile women after adjusting for age, residence and occupation (Favot *et al.*, 1997). An association was observed between past sexual behaviour and infertility problems, with infertile women having higher numbers of lifetime sexual partners, more marital breakdowns

and a higher level of exposure to sexually transmitted diseases. Another Ugandan study also showed that women with HIV infection were more likely to have a history of other STDs, which are a known cause of secondary infertility (Wagner *et al.*, 1994).

Another issue on which there is suggestive evidence, but only in a developed country setting, is the temporality of the effect of HIV on fertility. Lee found a significant effect of duration of infection on fertility among American women with AIDS (Lee *et al.*, 2000). The relative risk of giving birth fell from 0.85 (95% CI 0.71, 1.03) at 7½ to 10 years before an AIDS diagnosis to 0.45 (95% CI 0.38, 0.55) in the last 2½ years before the AIDS diagnosis. As the average time since infection is likely to lengthen as the epidemic matures, the magnitude of the HIV-associated fertility reduction could change with time.

This paper presents data from a large open cohort study in rural Tanzania between 1994 and 1998. It aims to provide further insights into the relationship between women's HIV status and fertility by analysing fertility differentials by HIV status and by comparing the HIV infection rates in pregnant women with those in all women regardless of pregnancy status. The dynamics of the relationship between HIV and fertility are also investigated, by looking at how fertility varies by duration and severity (in terms of proximity to death) of HIV infection.

Background and methods

This study was carried out in the Kisesa ward of Mwanza region of North-west Tanzania. The ward consists of a group of six dispersed villages and a slightly more urbanized centre, and forms an administrative entity in its own right. Kisesa ward has a population of approximately 20,000 and lies about 20 km east of Mwanza City, the regional capital, on the main road to Kenya. The Sukuma are the largest ethnic group in Kisesa, comprising more than 90% of the population. Farming is the main source of income.

In 1994, a demographic surveillance system was set up in Kisesa. Each household in the ward was visited and data on the demographic characteristics of all residents were collected. Every 6 months each household was revisited and this information was updated with new data about births and deaths among the residents and about migrations to and from the area. By the end of 1998 ten surveillance visits had been completed. In addition to demographic surveillance, an epidemiological survey was undertaken during 1994 and 1995 of all adults between the ages of 15 and 44. Eligible persons (i.e. all those born between 1950 and 1980 and listed as resident at a previous surveillance visit) were asked to come to a central point in the village to be interviewed with an extensive structured questionnaire. In addition, respondents were asked to provide a blood sample for HIV testing. The survey was repeated 2 years later, during 1996 and 1997, for all adults aged between 15 and 46 resident in the area. Attendance at the first and second surveys was 5820 (78.0%) and 6413 (79.5%) respectively (Boerma *et al.*, 1999). Details of the testing procedures used, along with more detailed information on the data collection methods and study population, have been published elsewhere (Boerma *et al.*, 1999).

Table 1. HIV prevalence by age and parity, both surveys combined

Age	Parity			
	0	1-2	3-5	6+
15-19	0.9	3.7	0.0	—
20-24	17.0	6.4	5.7	0.0
25-34	21.5	17.6	13.6	4.8
35+	23.1	9.2	7.2	6.0
Age adjusted	5.9	9.4	11.3	5.6

Results

All women aged between 15 and 44, who were resident in Kisesa and present at two or more demographic surveillance visits, are included in this fertility analysis. Data were obtained from 7631 women with a mean duration of follow-up of 29.6 months. Attendance at the two epidemiological surveys, among these women, was 2942 and 3308 in 1994-5 and 1996-7 respectively. The majority of women who did not participate in the surveys were not listed as resident in the demographic surveillance system at the time of the survey. The median age of the women was 26 years in the first survey and 27 years in the second. HIV results are available for all but seventeen of the women in the first survey and eleven in the second. This resulted in a total of 4139 women for whom at least one HIV test result was available. Female HIV prevalence at the two surveys was 6.7% and 7.9%. HIV incidence between the two surveys was 0.84 per 100 woman-years. HIV prevalence among men was lower at 5.0% and 5.1% at the first and second surveys respectively, and HIV incidence was 0.73 per 100 man-years.

Table 1 shows the background association between women's parity and HIV status for the two surveys combined. A clear pattern is seen with nulliparous women having the highest HIV prevalence at all ages with the exception of the 15-19 age group, where childlessness is strongly associated with low levels of sexual activity. Amongst teenagers, it is women of parity one and two who have the highest HIV prevalence, but outside of this age group, lowest HIV prevalences are seen at highest parities.

Fertility and HIV

Age-specific fertility rates (ASFRs) for women aged 15-44, by HIV status, are shown in Table 2. These have been computed on the basis of births occurring up to 2 years after the last HIV test. Three groups of women are compared. The first group are women who tested negative at both sero-surveys. The second group consists of those who were uninfected in 1994-5 but whose status in 1996-7 is unknown. The third group are women followed up after a serology test showed them to be infected. The inter-survey experience of the 33 women who sero-converted between the surveys has not been included in this analysis.

Table 2. Age-specific fertility rates per 1000 women-years, by HIV status in the two surveys, based on demographic surveillance data

Age group	Uninfected at 1st and 2nd surveys		Uninfected at 1st/unknown at 2nd survey		Infected or unknown at 1st/infected at 2nd survey	
	ASFR	Women-years	ASFR	Women-years	ASFR	Women-years
15-19	121	1998	82	368	166	30
20-24	292	1887	197	391	158	159
25-29	290	1718	211	284	152	243
30-34	256	1592	202	277	83	169
35-39	187	1329	87	139	55	91
40-44	91	1097	74	136	103	49
TFR	6.2		4.3		3.6	

The total fertility rate (TFR) in the second group of women was 4.3, closer to the rate for the initially infected than for those remaining negative throughout. This may appear surprising, given the relatively low rate of sero-conversion observed in the population, but women in this group are more mobile than those who were present for both rounds of HIV testing. Mobility is associated with having fewer family ties, including less stable marriage and lower fertility. Mobility and marital stability are both considered risk factors for HIV (Caldwell *et al.*, 1997; Ntozi, 1997; Boerma *et al.*, 2002).

Age-specific fertility rates were also calculated for another highly mobile group: the 3492 women aged 15-44 who were present at two or more demographic surveillance visits but who did not have an HIV test result from either sero-survey. Their ASFRs also fell between the rates of the women of known HIV status, and their total fertility rate was 4.8.

The age-adjusted fertility rate ratio was calculated, treating the women in both the first two categories in Table 2 as uninfected. The resulting age-adjusted fertility rate ratio was 0.71 for infected women compared with uninfected women.

HIV prevalence levels among all women aged 15-44 encountered in the two epidemiological surveys and among women who were known to have been pregnant during the inter-survey period are shown in Fig. 1. Women were classified as pregnant if they gave birth during the inter-survey period or in the subsequent 9 months. For women aged 20 and over, HIV prevalence was higher in both survey populations than among the subgroup of pregnant women. This difference is statistically significant among women aged 20-39. Among women aged 15-19, a higher HIV prevalence was found in pregnant women: 3.15% compared with 1.03% and 1.92% in all women at the first and second surveys respectively.

Fertility among HIV-infected women

The effect of duration of HIV infection on fertility was examined by looking at general fertility rates (GFR: births per 1000 women-years of observation) among

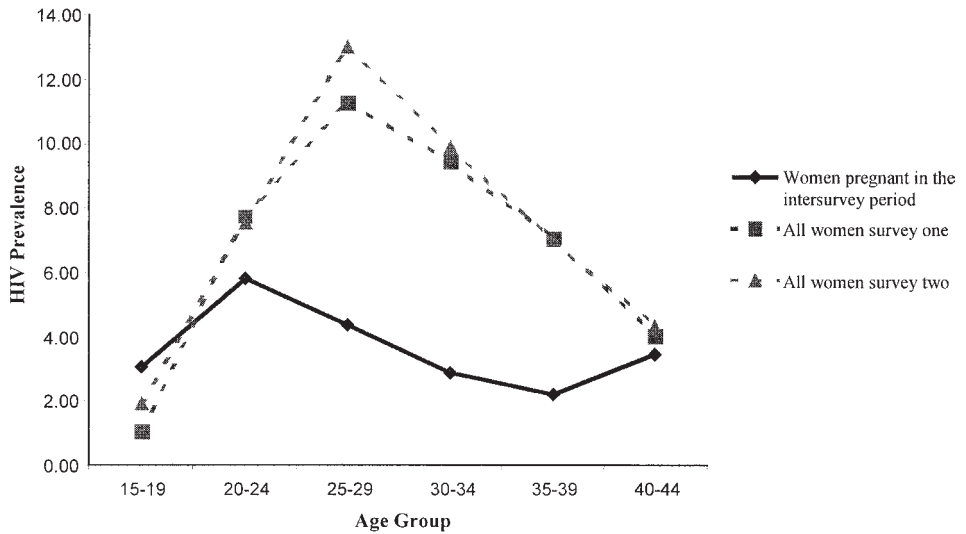


Fig. 1. HIV prevalence among all women at surveys one and two and among pregnant women in the inter-survey period.

Table 3. General fertility rates (per 1000 women-years, ages 15–44) by year since first HIV-positive test

Year	<i>n</i>	GFR
1	304	109.9
2	192	92.2
3	105	73.0
4	65	210.9

infected women by year since they first tested positive in this study, either in the first or second survey. The results are shown in Table 3. There is a suggestion of a modest downward trend in the GFR with increasing time since first positive HIV test, with the exception of the fourth year. However, the final year's estimate must be interpreted with caution. It is based on only 38 women-years' observation and is therefore prone to error, since the 65 women who survived for more than 3 years after testing positive had on average been observed for only half of the fourth year.

The effect of severity of infection on fertility was also investigated by comparing the GFR during the period 1994–1998 among 271 HIV-infected women who survived to the tenth surveillance visit with the GFR among 33 infected women who had died before this visit. The GFR among survivors was 112 (based on 53 births in 473.4 women-years of observation), compared with a GFR of 29 for women who died before the tenth round (who experienced one birth in the 34.2 person-years before they died). This large and significant difference gives an indication of the possible

Table 4. General fertility rates (per 1000 women-years, ages 15–44) by use of modern contraception and HIV status

HIV status	Current use of modern contraception					
	Non-users		Users		All women	
	GFR	Women-years	GFR	Women-years	GFR	Women-years
Negative	207.6	10,523	131.5	646	203.2	11,169
Positive	153.4	678	63.7	94	142.4	772
All women	204.4	11,201	122.9	740	199.3	11,941
Ratio +/-	0.74		0.48		0.70	

effect of HIV-associated illness on fertility. The effects of women's illness may also be compounded by illness and death among their partners, since women who died were more likely to have had partners at an advanced stage of HIV disease. At the time of the first survey, 6.4% of women were widowed in the population as a whole. Among the HIV-infected women, 17.4% of those who survived to the tenth surveillance visit were widowed compared with 25.0% of the women who died before this time.

Fertility control by HIV status

General fertility rates for women aged 15–44, by HIV status and use of modern contraception, are shown in Table 4. Contraceptive users are women who reported current use of modern contraception at either the first or second sero-surveys. Non-users consist of women who attended at least one of the two surveys and did not report current use of modern contraception at either survey. The 33 women who sero-converted between the two surveys have been excluded from this table. The proportion of women describing themselves as current users of contraception increased from 5% to 6% between the surveys, but around 10% of HIV-positive women were recorded as contraceptive users in both surveys. Current contraceptive use is almost twice as high among HIV-positive women, but clearly both HIV-positive and HIV-negative women do not use contraception consistently and continuously, since the fertility rates of contraceptive users, though substantially lower than those of non-users, are far from zero. Among both contraceptive users and non-users, a substantial fertility reduction was seen among HIV-infected women (52% and 26% respectively).

Discussion

In a rural area in North-west Tanzania, the fertility of HIV-positive women compared with HIV-negative women was reduced by 29%, after adjusting for differences in age distribution. This effect is slightly larger than that observed in other studies in sub-Saharan Africa (Ryder *et al.*, 1991; Sewankambo *et al.*, 1994; Carpenter *et al.*, 1997), but of the same order of magnitude.

Contrary to the differential at older ages, the ASFR among infected women in the age group 15–19 was 166 per 1000 women-years: higher than the rate of 121 recorded among uninfected women under 20. This pattern was also seen in two Ugandan studies: in Masaka (Carpenter *et al.*, 1997), and in Rakai (Gray *et al.*, 1998), but it was not possible to tell if this pattern occurred in the Kinshasa study (Ryder *et al.*, 1991) due to the age grouping of the results.

Several studies in sub-Saharan Africa have compared the prevalence of HIV among pregnant women from antenatal clinics with HIV prevalence among women in the community from a population-based survey. In six out of seven of these studies (Fort Portal, Uganda, 1998 (Kilian *et al.*, 1999), Mwanza Town, Tanzania, 1991 (Kigadye *et al.*, 1993; Kwesigabo *et al.*, 1996), Ndola, Zambia, 1998 (Musonda *et al.*, 1999), Kinshasa, Zaire, 1996 (Fylkesnes, *et al.*, 1998) and Yaounde, Cameroon, 1998 (Macauley *et al.*, 1999)), the ratio of HIV prevalence in pregnant women compared with that in all women ranged from 0.70 to 0.87. In one study carried out in Kisumu, Kenya, in 1998 (Kahindo *et al.*, 1999), the ratio was found to be 1.04. Attendance rates at the clinics were estimated to be over 85% in the studies in Fort Portal, Mwanza Town and Kinshasa. These rates are not available for the other studies. However, evidence from DHS surveys suggests that antenatal clinic attendance rates in these countries are of a similar order of magnitude. In the Kisesa study, the experience of all pregnant women is captured, regardless of antenatal clinic attendance, and the ratio of HIV prevalence in pregnant women to that of the general female population of childbearing age is 0.79.

The reduction in fertility among HIV-infected women may have behavioural and biological causes. Women with HIV infection may have less frequent sexual intercourse and many may not have intercourse at all, especially if they are affected by opportunistic infections or if their partners die of AIDS. This suspicion cannot be confirmed using the data from Kisesa, since detailed data on sexual intercourse were not collected. Women with HIV infection may also be more frequent users of contraceptive methods, including condoms. In this study contraceptive use rates among the HIV-positive were found to be double those of the HIV-negative. Very few women in the Kisesa population were aware of their HIV status during the study period. Less than 1% made use of the voluntary counselling and testing services during the 1996–97 survey. It is therefore unlikely that contraceptive use in this group was entirely motivated by awareness of infection status, although no information is available on which women made use of the testing in order to confirm this. Higher rates of contraceptive use among the HIV-positive do not explain the entire fertility differential, since the fertility difference between HIV-positive and HIV-negative women persists amongst contraceptive users. If contraceptive use rates had been the same in HIV-positive and HIV-negative women, the overall general fertility rate ratio would be little changed, increasing from 0.70 to 0.73.

Biological effects of HIV infection on fertility are likely to become stronger the longer the infection persists, as was observed in a US study (Lee *et al.*, 2000). The current study found little evidence of larger reductions of fertility over time, with the exception of the terminal year(s) of infection. An important limitation of this analysis is that women are only categorized as infected after their first positive HIV test result. No attempt is made to estimate a likely infection date. If the biological association

between duration of infection and fertility is non-linear, which seems plausible, this would have affected the results.

Ross *et al.* (1999) found in a study in rural Uganda that about half of the reduced fertility among HIV-infected women was associated with lower pre-existing fertility, and suggested this might be due to higher risk behaviour among women with subfertility (Favot *et al.*, 1997). In this study it was not possible to assess the potential confounding effect of subfertility prior to HIV infection on the association between HIV and fertility due to the small number of incident cases. HIV incidence among women with no birth in the last 5 years before the survey was not higher than that in women who gave birth in the last 5 years.

In summary, this study in rural Tanzania shows a substantial reduction in fertility among HIV-infected women compared with HIV-negative women. The fertility reduction was most pronounced during the terminal stages of infection, but no clear association with duration of infection was observed. To be able to assess to what extent behavioural or biological factors and subfertility prior to infection with HIV infection are responsible for the large differences observed in fertility of HIV-infected and uninfected women, more detailed data on sexual behaviour are needed, especially during the later stages of infection.

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