Decreasing HIV-1 seroprevalence in young adults in a rural Ugandan cohort

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Abstract

***Objective*—To assess the trend in HIV-1 seroprevalence in an adult population in Uganda.**

***Design*—An observational cohort study with four year follow up.**

***Setting*—A cluster of 15 villages in rural Uganda.**

***Subjects*—All residents of the 15 villages—about 10 000 people.**

***Main outcome measure*—Prevalence of HIV-1 infection as assessed by enzyme immunoassay.**

***Results*—During the five year period the overall standardised seroprevalence of HIV-1 showed little change; 8·2% in 1990, 7·6% in 1994. Among males aged 13-24 years the prevalence decreased from 3·4% to 1·0% (P for trend $<0·001$); among females of the same age the corresponding values were 9·9% and 7·3%. The decrease was greatest in males aged 20-24 years and females aged 13-19 years.**

***Conclusion*—This is the first report of a decline in HIV-1 prevalence among young adults in a general population in sub-Saharan Africa with high overall HIV-1 prevalence. It is too early to conclude that the epidemic in this population is in decline, but the results of this study should be reason for some cautious optimism and encourage the vigorous pursuit of AIDS control measures.**

Introduction

The HIV-1 epidemic continues to spread in Africa,[1] but some studies have reported unchanging HIV-1 prevalence among adult populations in different regions in Burundi, Rwanda, and Zaire.[2-6] In some of the major towns of Uganda the prevalence of HIV-1 among women attending antenatal clinics included in the national sentinel surveillance programme has declined since 1992; for example, the reported rates from the two main hospitals in Kampala, the capital city, fell from 29% to 22% in one hospital and to 17% in the other.[7]

The population dynamics which underlie the course of the HIV-1 epidemic are complex.[6] Sociodemographic, cultural, and biological factors play an important part, as does the effect of specific interventions, including behaviour change and promotion of condom use, counselling, and control of sexually transmitted diseases. In recent years encouraging results have been reported from sub-Saharan Africa on successful interventions in cohorts of women attending antenatal clinics,[8] and prostitutes[9 10]; but only one successful intervention has to date been reported for general populations in sub-Saharan Africa.[10a]

In 1989-90 we began a descriptive study of the population dynamics of HIV-1 by enrolling a rural population cohort in Uganda.[11-14] We report here the age and sex specific trends in HIV-1 prevalence during four years of follow up.

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BACKGROUND

The area of study is a cluster of 15 neighbouring villages containing about one third of the population of a subcounty of Masaka district in south west Uganda, situated about 32 km from Masaka town and 16 km from the trans-Africa highway at its nearest point. The inhabitants are mainly peasants who grow bananas as a subsistence crop and cultivate coffee for sale. Households are scattered, although some are concentrated around the trading village at the centre of the study area. The predominant tribal group, the Baganda, constitute approximately 70% of the population. Most people are Roman Catholics; about one quarter are Muslims. The area used to have two dispensaries and a health centre; in 1990 the research programme opened a study clinic.

The median age at first sexual contact is 15 years for women and 17 years for men.[15] Sexually transmitted diseases are common[11 16] and condoms are used relatively rarely.

As we set out to conduct an observational study, the AIDS control measures initiated by the programme were initially limited in scope and intensity and complemented general awareness campaigns of the national AIDS control programme. Measures initiated by the programme included health education efforts, a limited distribution of condoms, and improvement of control of sexually transmitted diseases.

Methods

Beginning in late 1989, after the study villages had been mapped, a census and socioeconomic questionnaire were administered to all consenting heads of household. All de jure residents were included. Two to three weeks later a medical team visited each of the households. All adults were invited to participate in the medical and serological survey, which involved a medical history and physical examination. A blood sample was taken from consenting adults and children. Details of the procedures have been described elsewhere.[12]

Blood specimens were transported at weekly intervals to the laboratory of the Uganda Virus Research Institute in Entebbe, where they were tested for antibodies to HIV-1 following a rigorous algorithm and quality control procedures.[17 18] In brief, all serum samples were tested by using two enzyme immunoassay systems: Recombigen HIV-1 enzyme immunoassay (Cambridge Biotech Corporation, Worcester, Massachusetts) and Wellcozyme HIV-1 Recombinant (Wellcome Diagnostics, Dartford) with western blot when indicated (this included all specimens from subjects positive for the first time; Novopath HIV Immunoblot, Bio-Rad Laboratories, Watford).

During 1990-4 the cohort was surveyed annually by using procedures similar to those at baseline. On each of these surveys newborns and those new to the area

were added to the cohort. A counselling service was available for those participants who wanted to know their HIV status.[19] Field staff were not aware of the HIV status of study participants.

Data were entered by double entry and verification, and data were checked for consistency. Existing software packages (EPI INFO and EGRET) were used for statistical analyses. In calculating significance of differences in prevalence or of trends in prevalence over time we used methods for non-matched data. As a consequence the reported P values underestimate true differences.

Results

At the initial survey there were 1981 households in the 15 study villages; 1806 (91·2%) of households agreed to take part in the census: a total population of 9777. Of 5226 adults (aged 13 years or more) 4167 (80%) were enrolled during the initial survey and had an unambiguous serostatus. After four years 89% of adults initially present had been enrolled. During the four year follow up period 28% of those present in the first survey left the area. Those remaining in the study area, leaving the study area, or joining from outside the area had 5·5%, 11·5%, and 16·3% progressively higher (standardised) rates of HIV-1 infection.[20] After four years the total adult population was 5649; 88% of these had had blood samples taken at some time and had an unambiguous serostatus.[17]

At the four follow up surveys the compliance rates among the resident population were 67%, 61%, 57%, and 62%. Non-compliance was not cumulative, however, and at four years 71% had an unambiguous serostatus at either the three year or the four year follow up. For young adults aged 13-24 the compliance rates were 62%, 56%, 52%, and 57% at the follow ups; of those resident at the fourth follow up, 88% had given a blood sample on one or more occasions.

Table I shows HIV-1 seroprevalence by survey round for the total adult population and by age and sex. During the five year period the overall age and sex standardised seroprevalence showed little change from 8·2% (95% confidence interval 7·4% to 9·1%) at round 1 to 7·6% (6·7 to 8·5) at round 5. There was, however, a considerable decrease in prevalence in males aged 13-24 years (from 3·4% to 1·0%; P for trend $<0·001$) and a suggestion of a corresponding decrease in females (from 9·9% to 7·3%; P for trend=0·08). Changes in other age groups were small.

The HIV-1 prevalence among those aged 13-24 years is more closely examined in table II. In the age group 13-19, seroprevalence in males was very low at both round 1 (0·2%) and round 5 (0·4%); in young adult females the rate fell from 4·5% (27/601) to 2·4% (13/531; P=0·09). In men aged 20-24 years rates declined from 11·8% (28/237) to 2·7% (5/187; $P<0·001$); there was little change among women of the same age.

TABLE I—*HIV-1 seroprevalence by age group, sex, and survey round rural cohort, Masaka, Uganda, 1989-94. Values are percentages (number positive/total) of subjects*

	Round 1	Round 2	Round 3	Round 4	Round 5
Males					
13-24	3·4 (29/846)	3·6 (26/716)	2·3 (15/657)	1·6 (10/637)	1·0 (7/688)
25-34	18·3 (64/350)	18·2 (54/296)	19·8 (57/288)	22·9 (63/275)	19·4 (61/314)
35-44	13·5 (30/223)	11·9 (23/194)	12·1 (24/199)	12·2 (22/181)	14·5 (29/200)
≥45	4·8 (27/561)	4·6 (22/483)	4·4 (20/452)	5·3 (22/419)	5·3 (23/435)
Females					
13-24	9·9 (87/883)	8·2 (68/833)	7·8 (61/778)	8·1 (56/691)	7·3 (54/742)
25-34	13·3 (57/429)	12·6 (50/396)	15·2 (57/374)	17·1 (63/369)	15·9 (60/377)
35-44	8·8 (26/294)	9·5 (23/243)	10·5 (25/238)	7·9 (17/215)	7·7 (18/234)
≥45	3·9 (23/586)	4·0 (20/501)	3·9 (17/439)	3·9 (16/406)	4·2 (14/452)
Total†	8·2 (343/4172)	7·8 (286/3662)	7·8 (276/3425)	8·1 (269/3193)	7·6 (271/3342)

†Percentages standardised for age and sex.

TABLE II—*HIV-1 prevalence in age groups 13-19 and 20-24 years, rural cohort, Masaka, Uganda, 1989-94. Values are percentages (number positive/total) of subjects*

	Round 1 (1989)	Round 5 (1994)	Difference in percentages (95% confidence interval)	P value
Males				
13-19	0·2 (1/609)	0·4 (2/501)	−0·2 (−0·1 to 0·4)	>0·5
20-24	11·8 (28/237)	2·7 (5/187)	9·1 (4·4 to 13·9)	<0·001
Total	3·4 (29/846)	1·0 (7/688)	2·4 (1·0 to 3·8)	<0·01
Females				
13-19	4·5 (27/601)	2·5 (13/531)	2·0 (−0·1 to 4·1)	0·09
20-24	21·3 (60/282)	19·4 (41/211)	1·9 (−5·3 to 9·0)	0·25
Total	9·9 (87/883)	7·3 (54/742)	2·6 (−0·2 to 5·3)	0·08

During the period 1989 to mid-1994 the incidence of HIV-1 infection among adults in the cohort remained at about 7/1000 person years (7·3 in 1989-91 and 7·1 in 1992-4; data not shown). There was a suggestion of a decrease in incidence among males aged 13-24 years from 6·4/1000 person years (7/1094) to 2·6/1000 (4/1530; P=0·14); however, among females of the same age the corresponding rates were 8·2/1000 (9/1100) and 9·7/1000 (14/1442; P=0·7).

At the initial survey there were 29 seropositive males and 87 seropositive females in the 13-24 year age group. In the following four years 75 (27 males, 48 females) moved into the next age group; 19 (all females) left the area and eight (1 male, 7 females) died. The remaining 14 (1 male, 13 females) were still present at the time of the fourth resurvey and aged less than 25 years.

Two (1 male, 1 female) seropositive children moved into the 13-24 year age group; 29 seropositive 13-24 year olds (3 male, 26 female) joined the cohort, 25 of these after moving into the area; and 19 (4 males and 15 females) seroconverted. Thus at the fourth follow up survey there were nine seropositive males and 55 seropositive females in the 13-24 year age group.

Discussion

During four year follow up of a rural Ugandan cohort we observed a significant decline in the prevalence of HIV-1 infection among males aged 13-24 and a non-significant reduction among young females but no such change in other age groups. This is the first time that a decline in HIV-1 prevalence is being reported for a sub-Saharan population.

POSSIBLE BIASES

Almost 90% of those aged 13-24 who were resident in the fourth year of follow up had given one or more blood samples, suggesting that enrolment bias was limited. The rates of non-compliance and of leaving the area were slightly higher for participants who were HIV-1 positive than for those who were negative, but there was no indication of an increase in these differences over time; only one seropositive man in the age group 13-24 left the area. Those aged 13-24 years who were included in the census but who did not give a blood sample had a higher mortality (16·8/1000 person years compared with 6·2/1000 among those participating), a finding in support of selective non-compliance; this group counted, however, for only 11% of the person years of observation.

The HIV testing algorithm and quality control procedures remained unchanged during the course of the study.[17,18] Errors in the ascertainment of serostatus cannot be totally excluded, but is is unlikely that they changed over time.

Thus, although selective enrolment and non-

compliance may well have resulted in an underestimate of the absolute prevalence of HIV, there is no indication that there have been major changes in these differentials over the five years of the study and it is improbable that any biases have distorted the main finding of the study—namely, the substantial decline in HIV prevalence among young males.

PREVALENCE PATTERNS

The transmission of HIV-1 among adults in this population is almost exclusively through heterosexual contact,[21] and virtually no cases of HIV-1 infection are found in males aged 17 years or less and females aged 13 years or less. The prevalence of HIV-1 infection in young adults should therefore closely reflect recent incidence rates of HIV infection and be sensitive to changes over time. Thus, assuming a non-differential reduction in the force of infection, we would expect to see the largest changes in prevalence in 20-24 year old males and 13-19 year old females. This is consistent with our observations.

When mortality, mobility, age effects, and incidence are taken into account, the decline in seroprevalence in 13-24 year old males seems to be explained largely by the effect of aging and a low incidence. In comparison, the pattern among young females is more mixed: a smaller aging effect, a substantial mortality (presumably since women are infected at a younger age), a higher incidence, and a high rate of joining and leaving the area. The resulting modest decrease in seroprevalence in females aged 13-24 years masks the substantial decline in prevalence among 13-19 year old females.

EXPLAINING THE DECLINE

Study and intervention effects, or a combination of these, may have contributed to the decline in HIV prevalence. At the start of the study the programme recruited about 50 people from the subcounty, and an additional 40 technical and support staff were brought in and accommodated on a permanent basis. A field office, clinic, and laboratories were set up, and there is little doubt that the presence of the programme had a high profile in this rural area. The taking of blood samples caused considerable anxiety among the study population and stimulated heated discussions. Moreover, the start of the study happened to coincide with a rapid increase of deaths associated with HIV infection among long term residents. It is probable, therefore, that a study effect did operate.

The observed decline cannot be explained by lack of replacement of subjects at high risk. In a closed cohort the incidence of HIV-1 infection, in the absence of other effects, may decrease rapidly with time as subjects at highest risk of HIV infection become infected and are not replaced[22]; however, the group of young adults who are just entering sexually active life are effectively an open cohort with a high rate of replacement.

Intervention efforts aiming at reducing the frequency of partner change, distribution and promotion of condoms, and the control of sexually transmitted diseases were gradually expanded. The effect of these efforts was not evaluated. Messages to reduce the frequency of partner change were initially delivered during community meetings, and AIDS awareness was promoted through song and drama competitions at schools. From 1992 onwards efforts to change behaviour became more intense and used community health workers, traditional birth attendants, and women and adolescent peer groups. Condoms were distributed on a limited scale. Community based condom promotion and distribution through peer networks started in 1993; by mid-1994 its scale was still very limited. Sexually transmitted diseases are common in this population.[16] Measures for control of sexually transmitted diseases, introduced in late 1990, included free treatment, notification of contacts, and efforts to influence the population's patterns of seeking treatment; even so, only a relatively small proportion of people with symptomatic sexually transmitted diseases sought treatment in the official health sector (H U Wagner *et al*, sixth international conference on AIDS in Africa, Dakar, 1991). On balance, though, it seems reasonable to assume that the intervention efforts initiated by the programme, together with the activities of the national AIDS control programme, will have had an impact.

Key messages

- Some reports suggest that the AIDS epidemic may be stabilising in some African countries
- This observational cohort study of a rural population in Uganda shows an overall stable prevalence
- A significant decline in the prevalence of HIV-1 among young adult males was observed; there was a suggestion of a corresponding decrease in young females
- These findings should encourage the vigorous pursuit of AIDS control measures

The most important result of this study is the observation that a decrease in infection rates among young adults is possible, even in populations with a relatively high force of HIV infection, with no more than a modest intensity of interventions. To determine if the transmission of HIV-1 has also decreased among older age groups will require a longer term cohort follow up. Even if there was no effect on the incidence in older age groups, a reduction in the prevalence of infection among young adults is undoubtedly a public health benefit.

Although in our study the decline in prevalence was less in women than in men, the observed decline is consistent with the recent results of the national antenatal surveillance system,[7] suggesting that the epidemic may be levelling off in at least some rural and urban areas in Uganda. It is too early to conclude that the epidemic is in decline, but the results of this study should be reason for cautious optimism and encourage the vigorous pursuit of AIDS control measures.

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Morbidity and severity of illness during interhospital transfer: impact of a specialised paediatric retrieval team

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Abstract

***Objective*—To evaluate the morbidity and severity of illness during interhospital transfer of critically ill children by a specialised paediatric retrieval team.**

***Design*—Prospective, descriptive study.**

***Setting*—Hospitals without paediatric intensive care facilities in and around the London area, and a paediatric intensive care unit at a tertiary centre.**

***Subjects*—51 critically ill children transferred to the paediatric intensive care unit.**

***Main outcome measures*—Adverse events related to equipment and physiological deterioration during transfer. Paediatric risk of mortality score before and after retrieval. Therapeutic intervention score before and after arrival of retrieval team.**

***Results*—Two (4%) patients had preventable physiological deterioration during transport. There were no adverse events related to equipment. Severity of illness decreased during stabilisation and transport by the retrieval team, suggested by the difference between risk of mortality scores before and after retrieval ($P < 0.001$). The median (range) difference between the two scores was 3·0 (−6 to 17). Interventions during stabilisation by the retrieval team increased, demonstrated by the difference between intervention scores before and after retrieval, median (range) difference between the two scores being 6 (−8 to 38) ($P < 0.001$).**

***Conclusions*—Our study indicates that a specialised paediatric retrieval team can rapidly deliver intensive care to critically ill children awaiting transfer. Such children can be transferred to a paediatric intensive care unit with minimal morbidity and mortality related to transport. There was no deterioration in the clinical condition of most patients during transfer.**

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Introduction

The improved outcome of critically ill children managed in paediatric intensive care units has increased the pressure to transfer such patients to a tertiary centre.[1] The risk of deterioration from the primary illness, complications of treatment, and the transfer process itself make the interhospital transfer potentially hazardous.[2-4] Unfortunately, despite recommendations, many critically ill children in the United Kingdom are still being transferred by non-specialised staff.[5-7]

There are no published data on the morbidity associated with transfer by a specialised paediatric retrieval team in the United Kingdom.

Patients and methods

This prospective, descriptive study at St Mary's Hospital, London, evaluated 78 consecutive patients transferred to the paediatric intensive care unit between October 1993 and May 1994. Fifty one patients were included in the study. Insufficient data from before retrieval prevented analysis of severity of illness in the 27 patients excluded from the study. In none of the patients excluded from the study was there any morbidity or mortality during transport.

The retrieval team consisted of a paediatric intensivist (senior registrar or consultant grade) and an experienced intensive care nurse.

ASSESSMENT OF MORBIDITY

Morbidity during transport was documented by using the criteria of Kanter and Tompkins (box).[2] Transport was defined as the period between leaving the referring hospital and arrival of the patient at the paediatric intensive care unit.

QUANTIFYING SEVERITY OF ILLNESS AND THERAPEUTIC INTERVENTIONS

To assess changes in severity of illness we used the paediatric risk of mortality (PRISM) score.[8] This score has been used as an index of severity of illness during interhospital transfer.[2 9-11]

For each child we computed the score at three points in time:

- The admission score by using values obtained on admission to the referring hospital