

Age Differences in Sexual Partners and Risk of HIV-1 Infection in Rural Uganda

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Objectives: To assess whether differences in age between sexual partners affect the risk of HIV infection in female adolescents and young adults.

Methods: A total of 6177 ever sexually active women aged 15 to 29 years completed a sociodemographic and sexual behavior questionnaire and provided a blood sample for HIV-1 serology. The age difference between partners was categorized as men 0 to 4 years older (referent group), 5 to 9 years older and 10 or more years older. HIV prevalence and incidence were assessed, and adjusted RR was estimated by multivariate regression.

Results: Prevalent HIV-1 infection in female participants increased with older male sexual partners. Among women aged 15 to 19 years, the adjusted risk of HIV infection doubled (RR = 2.04; 95% CI: 1.29–3.22) among those reporting male partners 10 or more years older compared with those with male partners 0 to 4 years older; among women 20 to 24 years of age, the RR was 1.24 (95% CI: 0.96–1.60). The attributable fraction (exposed) of prevalent HIV infection in women aged 15 to 24 years associated with partners 10 or more years older was 9.7% (95% CI: 5.2–14.0). HIV incidence did not increase with differences in age of partners.

Conclusion: The age difference between young women and their male partners is a significant HIV risk factor, suggesting that high HIV prevalence in younger women is caused, in part, by transmission from older male partners.

Key Words: HIV—Adolescence—Sexual partners—Uganda.

Gender differentials in HIV prevalence and incidence among adolescents and young adults have been observed

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in studies from Uganda (Fig. 1) (1–4) and other sub-Saharan Africa countries (5–7). Female adolescents are, on average, eight times more likely to be HIV infected than male adolescents. Biologic mechanisms such as immaturity of the reproductive tract in younger women may increase susceptibility to HIV acquisition, and social and cultural practices that promote early sexual activity among women may also be important. Another hypothesized factor is that young women are infected by having sex with older men, who may be more likely to be infected (8–10). This assumption is supported by comparison of age-adjusted HIV prevalence data (4,5,11) and mathematic modeling (12,13). Few empiric studies have examined the effect of age differences between partners on the risk of HIV infection in young women, however (2,14,15). We undertook observational analyses of the sexual behavior characteristics of adolescents in Rakai District, Uganda, to assess the extent to which the age

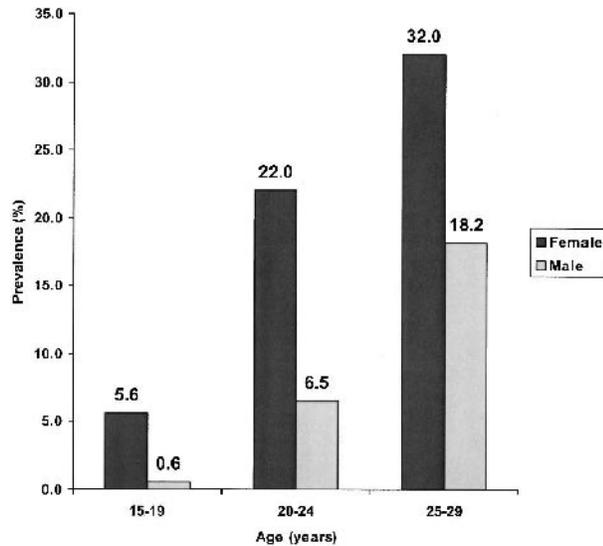


FIG. 1. HIV prevalence by gender and age.

differences between sexual partners affect the risk of HIV infection.

METHODS

We conducted a randomized community-based trial on the control of sexually transmitted diseases (STDs) for AIDS prevention in 56 communities of rural Rakai District, Uganda, between 1994 and 1998. The design and results of this trial have been described elsewhere (16,17). Consenting resident adults aged 15 to 59 years were enrolled in the study. Same-sex interviewers administered a questionnaire on socio-demographic characteristics and behaviors and collected samples for HIV testing and STD diagnosis. Detailed information was obtained on current and previous relationships, including characteristics of sexual partners, number of partners in the previous year and previous 5 years, use of condoms, and AIDS-related knowledge and attitudes.

Individuals were informed that participation in the study was voluntary, that all data and results were confidential, and that on their request, they would be given their HIV test results and free HIV counseling provided by trained project counselors. The project was reviewed and approved by the two institutional review boards in Uganda and two in the United States.

In this open cohort, baseline data were collected at the first survey round between November 1994 and August 1995, and for new enrollees (including in-migrants and newly age-eligible individuals), data were collected at three subsequent surveys conducted at 10-month intervals. Follow-up surveys provided prospective data for estimation of HIV incidence. Venous blood was collected for serologic diagnosis of HIV using two different enzyme immunoassays (Vironostika HIV; Organon Teknika, Charlotte, NC, U.S.A. and Cambridge Biotech, Worcester, MA, U.S.A.), with Western blot confirmation of discordant enzyme immunoassay results and seroconversions (HIV WB; Bio-Merieux-Vitek, St. Louis, MO, U.S.A.).

This report examines the risk of HIV infection associated with age differentials between an index woman and her most recent reported sexual partner. The differences in age were examined as a continuous variable and categorized into three groups: male age 0 to 4 years older (the referent group), 5 to 9 years older, and 10 or more years older. Our

focus was to assess the risk of older primary sexual partners, and the relationships we examined were restricted to the most recent sexual partner, because the majority of women reported only 1 lifetime sexual partner, particularly so among the 15- to 19-year-old age group, and less than 4% of women reported more than 1 sex partner within the preceding year.

Females with younger male partners were considered as a separate group because of small numbers. Marital status was classified as currently in union (i.e., religious and legal marriage or consensual relationship that includes cohabitation and informal marriage), women who were never married, or women who were previously married (i.e., widowed, divorced, or separated). We report on 6177 ever sexually active female participants between the ages of 15 and 29 years who completed a questionnaire and provided at least one blood sample for HIV-1 serology. A subgroup of 131 women who reported sexual relationships with younger male partners was later removed from this analysis. We estimated the prevalence of HIV infection associated with sociodemographic and behavioral risk factors of the woman and the age differential of her male partner using unadjusted HIV prevalence risk ratios (PRRs) and 95% CI. Tests of statistical significance used the 95% CI of the PRR and χ^2 tests. Log-binomial multivariate regression was used to estimate adjusted RRs of HIV infection associated with age differences of most recent partners (18,19). These models were adjusted for age, duration of the sexual relationship, number of sex partners in the previous year, marital status, and religion, all of which were found to be significantly associated with HIV-1 infection in bivariate analyses. Goodness of fit was assessed by the log-likelihood ratio (20). The attributable fraction (AF) for the exposed population was used to estimate the proportion of excess risk of HIV associated with varying age differences between sexual partners (21–23). The AF is applied to the “population” of female participants aged 15 to 29 years, because this is the population of primary interest.

To assess the risk of HIV seroconversion associated with the age difference between sexual partners, we determined HIV incidence per 100 person-years (PY) during the interval of seroconversion risk. The most recent partner was used throughout the incidence analysis; thus, if women changed partners, the age difference used was that for the partner at the beginning of each interval of risk. In most cases, this was the only partner and predominantly a spouse. The crude RRs and 95% CIs of incident HIV were estimated. Poisson multiple regression models (24) were used to estimate adjusted risks of seroconversion, adjusting for possible confounding by number of sexual partners in the previous year. All analyses used the SAS statistical package (SAS version 8.0; Cary, NC, U.S.A.).

RESULTS

Prevalence Study

Among 6177 ever sexually active women between the ages of 15 and 29 years enrolled at baseline, HIV prevalence was 20.0%. Female and male HIV prevalence rates between the ages of 15 and 29 years are shown in Figure 1. Compared with men, there was an excess of infection among women aged 15 to 29 years: at the age of 15 to 19 years, the PRR was 8.96 (95% CI: 5.38–14.90), at the age of 20 to 24 years, the PRR was 3.39 (95% CI: 2.83–4.07), and at the age of 25 to 29 years, the PRR was 1.76 (95% CI: 1.55–1.99). Figure 1 and Table 1 show that the

TABLE 1. HIV seroprevalence by risk factors for females, ages 15–29 (n = 6177)

Risk factor	N	HIV prevalence %	Unadjusted PRR (95% CI)
Age			
All	6177	19.7	
15–19 years	2195	7.6	1.0
20–24 years	2370	22.3	2.93 (2.49, 3.96)
25–29 years	1612	32.1	4.22 (3.59, 4.97)
Marital status			
Never married	1188	14.7	1.0
In union	4285	18.1	1.23 (1.06, 1.43)
Separated/divorced/widowed	511	45.0	3.06 (2.59, 3.61)
Education			
None	563	18.7	1.0
Primary	4123	20.7	1.0 (0.84, 1.21)
Secondary	1314	17.1	0.77 (0.62, 0.95)
Tertiary	177	18.6	1.01 (0.71, 1.43)
Religion			
Muslim	903	15.8	1.0
Non-Muslim	5274	20.3	1.28 (1.09, 1.50)
No. of sexual partners in past 5 years			
1	4095	15.7	1.0
2+	2003	27.6	1.76 (1.59, 1.94)
Duration of relationship			
0–4 years	4284	18.7	1.0
5+ years	1874	21.9	1.17 (1.06, 1.30)

PRR, prevalence risk ratios; CI, confidence interval.

prevalence of HIV-1 increased with age from 7.6% in women aged 15 to 19 years, to 22.3% in 20- to 24-year-olds, and to 32.1% in 25- to 29-year-olds.

The mean age of first marriage was 19.3 years (25). The median age at first sex was 15 years for 15- to

19-year-olds and 16 years for women aged 20 to 29 years. HIV-1 infection among women in union was higher than that in never-married women, 18.1% and 14.7, respectively (RR = 1.23; 95% CI: 1.06–1.43). High rates of infection were found in the separated, divorced, or widowed women (45.0%). There was a significant increase in HIV prevalence for those with 2 or more sexual partners in the past 5 years. HIV infection was significantly higher in those who had reported being in sexual relationships that lasted longer than 5 years compared with those whose relationships were between 0 and 4 years in length (Table 1). HIV rates did not differ significantly by level of education. HIV infection was significantly higher in non-Muslim women than in Muslim women (RR = 1.28; 95% CI: 1.09–1.50).

The median age was 24 years for HIV-positive women and 20 years for HIV-negative women ($P = 0.0001$). The mean age difference between the HIV-negative women and their older male partners was 5.7 years (95% CI: 5.58–5.91), whereas for HIV-positive women, the mean age difference between partners was 6.3 years (95% CI: 5.95–6.66). This partner age differential between HIV-positive and HIV-negative couples was statistically significant ($P = 0.002$).

Table 2 shows the association between HIV prevalence and the age difference between the index women and their most recent sexual partner. The risk of HIV-1 infection increased as the age difference widened. Relative to women with partners 0 to 4 years older, the adjusted PRR of HIV for women with partners 10 or more

TABLE 2. HIV seroprevalence associated with age difference of sexual partners in 15–29-year-old females: unadjusted and adjusted prevalence risk ratios

Age	Partner's age	N	HIV prevalence %	Unadjusted PRR (95% CI)	Adjusted PRR ^a (95% CI)
All	Younger males	193	32.1	2.23 (1.60, 3.12)	^b
	0–4 years older	2127	17.5	1.0	1.00
	5–9 years older	2171	19.1	1.09 (0.96, 1.23)	1.10 (0.95, 1.28)
	10+ years older	875	23.2 ^c	1.32 (1.14, 1.54)	1.28 (1.07, 1.52)
15–19	Younger males	14	7.1	1.20 (0.03, 8.31)	^b
	0–4 years older	883	6.0	1.0	1.00
	5–9 years older	745	6.9	1.14 (0.79, 1.65)	1.02 (0.69, 1.53)
	10+ years older	219	14.6 ^c	2.43 (1.61, 3.68)	2.04 (1.29, 3.22)
20–24	Younger males	53	24.5	1.26 (0.62, 2.51)	^b
	0–4 years older	741	20.5	1.0	1.00
	5–9 years older	908	21.6	1.05 (0.87, 1.27)	1.11 (0.90, 1.38)
	10+ years older	378	25.7 ^d	1.25 (1.00, 1.56)	1.24 (0.96, 1.60)
25–29	Younger males	126	38.1	1.23 (0.80, 1.87)	^b
	0–4 years older	503	33.4	1.0	1.0
	5–9 years older	518	32.2	0.97 (0.81, 1.15)	1.19 (0.96, 1.46)
	10+ years older	278	26.6 ^d	0.80 (0.63, 1.00)	0.91 (0.69, 1.19)

^a Adjusted log binomial regression; model includes number of sex partners in past 5 years, marital status, religion, duration of relationships.

^b Adjusted analysis not shown.

^c χ^2 for trend, $P < 0.001$.

^d χ^2 for trend, $P = 0.05$.

years older was 1.28 (95% CI: 1.07–1.52). HIV risk associated with the age difference between partners was greatest among women aged 15 to 19 years with male partners 10 or more years older (adjusted PRR = 2.04; 95% CI: 1.29–3.22) and women aged 20 to 24 years with partners 10 or more years older (adjusted PRR = 1.24; 95% CI: 0.96–1.60). The age difference in partners was not associated with HIV risk in women aged 25 to 29 years (adjusted PRR = 0.91; 95% CI: 0.69–1.19), however. As a result of missing data in the construction of the age difference variable, $n = 5173$ in Table 2.

The proportion of women with partners 10 or more years older increased with age from 11.8% in 15- to 19-year-olds, to 18.6% in women aged 20 to 24 years, and to 21.4% in women aged 25 to 29 years. The AF (exposed) of prevalent HIV associated with age differences in sexual partners was assessed for women less than 25 years old with 1 lifetime partner (Table 3). The adjusted AF was significantly increased in women with male partners 10 or more years older (AF = 9.7%; 95% CI: 5.2–14.0). Higher AFs were observed in 15- to 19-year-olds (AF = 12.4%; 95% CI: 2.2–21.5) than in 20- to 24-year-olds (AF = 5.1%; 95% CI: -0.2 to 10.2). Among married women, the adjusted AF was higher and statistically significant for 15- to 19-year-olds (AF =

13.8%; 95% CI: 0.2–25.6) and for 20- to 24-year-olds (AF = 7.3%; 95% CI: 0.5–13.6), whereas the AFs for single women were not significantly elevated.

Although not reported in detail in this article, we conducted a similar analysis for men reporting on their female partners. Briefly, we found that men are more likely to be infected with HIV as the age gap with their younger female sexual partners grows. This trend is statistically significant ($P = 0.0001$). Stratified by age groups, however, this trend disappears in the men. The lack of a stronger age difference effect in the men may be a result of the limitation of the study sample to men less than 30 years of age. It is probable that there are a substantial number of men older than 30 years of age having relationships with younger women who need to be included.

HIV Incidence

Table 4 shows the association between sexual partner age differences and HIV acquisition. Follow-up data were available on 5306 HIV-negative females. Overall HIV incidence was 2.1 per 100 PY. HIV incidence rates decreased with greater age differences between sexual partners, but these differences were not statistically sig-

TABLE 3. HIV seroprevalence associated with age difference of sexual partners in 15–24 year old females reporting one sexual partner, by marital status: prevalence risk ratios and attributable fraction (exposed)

Age	Marital status	Partner's age	N	HIV prevalence %	Proportion of cases exposed	Adjusted PRR	Adjusted attributable fraction % (95% CI)
15–24	All	0–4 years older	1101	8.8	43.6	1.0	—
		5–9 years older	1094	11.4	43.3	1.30	9.4 (0.03, 17.8)
		10+ years older	333	18.0	13.1	2.08	9.7 (5.2, 14.0)
	Single	0–4 years older	388	6.2	67.2	1.0	—
		5–9 years older	160	7.5	27.7	1.22	5.0 (-13.8, 20.7)
		10+ years older	29	13.8	5.1	2.22	4.7 (-3.0, 6.0)
	In union	0–4 years older	637	9.0	35.4	1.0	—
		5–9 years older	881	11.6	48.9	1.30	10.2 (-2.5, 21.4)
		10+ years older	284	17.3	15.8	1.96	10.2 (4.3, 15.7)
15–19	All	0–4 years older	645	3.9	52.0	1.0	—
		5–9 years older	481	4.2	38.8	1.12	3.6 (-17.3, 20.7)
		10+ years older	115	10.4	9.2	2.91	12.4 (2.2, 21.5)
	Single	0–4 years older	299	3.3	75.7	1.0	—
		5–9 years older	85	1.2	21.5	0.35	-14.1 (-34.1, 2.9)
		10+ years older	11	18.2	2.8	5.97	10.1 (-4.5, 22.7)
	In union	0–4 years older	310	4.2	39.3	1.0	—
		5–9 years older	378	4.8	48.0	1.20	7.1 (-24.6, 30.7)
		10+ years older	100	10.0	12.7	2.69	13.8 (0.2, 25.6)
20–24	All	0–4 years older	456	15.8	35.4	1.0	—
		5–9 years older	613	17.1	47.6	1.08	3.1 (-7.9, 12.9)
		10+ years older	218	22.0	16.9	1.40	5.1 (-0.2, 10.2)
	Single	0–4 years older	89	15.7	48.9	1.0	—
		5–9 years older	75	14.7	41.2	0.98	-6.6 (-27.8, 20.7)
		10+ years older	18	11.1	9.9	0.73	-2.4 (-12.6, 6.8)
	In union	0–4 years older	327	13.5	32.3	1.0	—
		5–9 years older	503	16.7	49.6	1.25	8.7 (-5.2, 20.7)
		10+ years older	184	21.2	18.2	1.56	7.3 (0.5, 13.6)

PRR, prevalence risk ratio; CI, confidence interval.

TABLE 4. Incidence rate ratio (RR) of age difference of sexual partners associated with HIV serostatus for females by age (15–29 years)

Age	Partner's age	Number of HIV cases/person-year	HIV incidence/100 person-years	Crude RR (95% CI)	Adjusted RR ^a (95% CI)
All	All	143/6717	2.1		
	0–4 years older	45/1996	2.3	1.0	1.0
	5–9 years older	53/2371	2.2	0.99 (0.67, 1.48)	0.95 (0.63, 1.45)
	10+ years older	13/881	1.5	0.65 (0.34, 1.18)	0.62 (0.31, 1.14)
15–19	All	49/2749	1.8		
	0–4 years older	17/794	2.1	1.0	1.0
	5–9 years older	14/817	1.7	0.80 (0.39, 1.62)	0.81 (0.38, 1.68)
	10+ years older	3/188	1.6	0.75 (0.17, 2.22)	0.70 (0.16, 2.15)
20–24	All	58/2377	2.4		
	0–4 years older	13/730	1.8	1.0	1.0
	5–9 years older	27/991	2.7	1.53 (0.81, 3.06)	1.50 (0.77, 3.10)
	10+ years older	7/373	1.9	1.05 (0.40, 2.57)	1.09 (0.41, 2.72)
25–29	All	36/1591	2.3		
	0–4 years older	15/472	3.2	1.0	1.0
	5–9 years older	12/564	2.1	0.67 (0.31, 1.43)	0.52 (0.23, 1.15)
	10+ years older	3/321	0.9§	0.29 (0.07, 0.89)	0.18 (0.03, 0.65)

^a Model includes: number of sex partners in past 1 year.

^b χ^2 for trend, $P < 0.05$.

nificant in the 15- to 19-year-old and 20- to 24-year-old age groups. Multivariate Poisson regression models, adjusting for number of sexual partners in the past year and duration of relationships, showed a reduced risk of incident HIV that was statistically significant among women aged 25 to 29 years with partners 10 or more years older.

We also found the duration of the sexual relationship to be important. HIV incidence was 2.3 per 100 PY with a duration of the relationship from 0 to 4 years compared with an incidence of 1.8 per 100 PY with relationships of 5 years or more (RR = 1.50; 95% CI: 1.13–2.01).

DISCUSSION

The majority of women aged 15 to 29 years (98.2%) had relationships with men who were of the same age or older. There was a consistent association between older age of sexual partners and HIV-1 prevalence among women aged 15 to 19 years and 20 to 24 years but not among women aged 25 to 29 years (Tables 2 and 3). The association was greatest among female adolescents with partners 10 or more years older (RR = 2.43; 95% CI: 1.61–3.68) and was also significant for married female adolescents. Additionally, we found that the 1.8% of women with younger male partners had a high HIV prevalence compared with women whose partners were of the same age or older.

By the age of 15 years, half of all female adolescents had begun sexual activity, and by the age of 19 years, half were in marital or permanent consensual unions. Our findings for age of sexual debut and marital status concur with earlier Rakai studies (2) and with other reports from

rural Africa (26,27). The implication is that the high rates of HIV infection in female adolescents and women aged 20 to 29 years are a result of the early onset of sexual activity. Increased age of the male partner also contributed to rates of infection in young women, however. Seventeen percent of the women were in relationships with men 10 or more years older, and such older men are more likely to be infected with HIV (Fig. 1). Estimates of the AF (Table 3) suggest that 12.4% of the HIV prevalence in 15- to 19-year-olds and 5.1% of the prevalence in 20- to 24-year-olds can be attributed to relationships with men 10 or more years older, largely within marital relationships. Among HIV-infected women 15 to 19 years of age, 88.5% were ever married compared with 66.4% of HIV-negative women aged 15 to 19 years. This suggests that many of the HIV-positive female adolescents were infected by an older husband. Research in Zimbabwe and Uganda found that older men with higher incomes are more attractive as potential husbands to young women concerned about their financial security (14,28). In general, adolescent boys are not in a position to provide the expected financial support or to make suitable husbands, so women were drawn into relationships with older men. HIV interventions need to address these economic and cultural factors.

We did not observe an increase in HIV incidence among women with older male partners (Table 4). In fact, incidence declined significantly with increasing differentials in partner age for women aged 25 to 29 years. This apparent paradox, compared with the higher HIV prevalence associated with greater age differentials (Table 2), may be explained by the selection of the popu-

lations at risk for seroconversion. Because women with older male partners have higher HIV prevalence, there are selectively fewer HIV-negative women still at risk for incident HIV infections. Also, these women who previously avoided infection may be at lower risk (for biologic or behavioral reasons) and thus less likely to seroconvert during follow-up. There is a significant reduction in the proportion of HIV-negative women who remain at risk for seroconversion as the age difference between partners widens, with 84.6% at risk for women with partners 0 to 4 years older, 83.9% for those with partners 5 to 9 years older, and 80.2% for those with partners 10 or more years older (χ^2 for trend = 10.11; $P = 0.0015$).

In conclusion, this study has shown the importance of age differences between partners as a risk factor for HIV acquisition in young women, particularly young married adolescents. The age differences between women and their male partners cannot fully account for the excess HIV infections in young women relative to young men in the Rakai population, however. Similar studies of older male sexual partners have similarly concluded that the "age gap" provides only a modest explanation of the increased HIV risk among female adolescents (K. M. Becker, personal communication) (15). Further research into the attitudes, behaviors, and physiologic characteristics of this group and their partners is warranted.

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