Human Immunodeficiency Virus and Malaria in a Representative Sample of Childbearing Women in Kigali, Rwanda

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In 1986–1987 a consecutive sample of 3702 women presenting to prenatal and pediatric clinics at the only hospital in Kigali, Rwanda, was screened for human immunodeficiency virus (HIV) and malaria infection. The prevalence of HIV antibodies was 29%, and that of malaria parasites was 9%. HIV antibodies were more prevalent in women from the urban center than in those from the outskirts (31% vs. 20%, $P < .001$), and malaria parasites showed the opposite prevalence pattern (8% vs. 15%, $P < .001$); after stratifying by location, there was no association between HIV and the presence or degree of malaria parasitemia. HIV prevalence was 45% in women who had received a blood transfusion between 1980–1985 (before screening of donated blood began), and 28% among the great majority (94%) who had never been transfused. HIV prevalence was 44% in single mothers, 34% in women in common law unions, and 20% in those in legal marriages. These high rates of infection in the general population of Kigali highlight the need to develop effective programs for preventing further spread of sexually transmitted HIV.

Infection with the human immunodeficiency virus (HIV) is widespread in east and central Africa [1–15]. Although the infection has remained rare in most rural areas [16–18], it has become common in many cities. In Rwanda, a national HIV serosurvey in December 1986 found the prevalence of HIV antibodies to be 1% among rural inhabitants and 18% among those living in the cities [19, 20]; among urban dwellers aged 26–40 years, the prevalence was 30%.

HIV and malaria share regions of endemicity in Africa, and there may be an association between the two infections. Early studies showed a relationship between antibodies to HIV and to *Plasmodium falciparum* [21, 22], but a later report suggests that this may have been due to cross-reactivity and difficulty with interpretation of HIV–Western blot banding patterns [23]. Another study showed increased HIV infection rates in hospitalized children with a history of malaria, but this association was due to transfusions received for malaria-induced anemia [24, 25]. Neither these nor other studies of the topic [26, 27] have resolved the question as to whether infection with HIV predisposes to more frequent, longer, or more severe malaria parasitemia.

We studied a representative sample of childbearing women recruited from prenatal and pediatric clinics in Kigali, the capital city of Rwanda. This report analyzes the relationships among HIV antibodies and malaria parasitemia, history of transfusion, and demographic variables.

Methods

Sampling. Between October 1986 and March 1987, consecutive women aged 18 to 35 years and presenting to prenatal care or pediatric outpatient clinics at the Centre Hospitalier de Kigali were enrolled. This is the only community hospital in the city and is used by most Kigali women. There are good roads and buses in the city, and most of the women lived within 10 km of the hospital. The rate of refusal or incomplete data was 5%, yielding a study sample of 3702 women who are reasonably representative of the population of 18- to 35-year-old childbearing women in Kigali.

Measurements. An interviewer-administered questionnaire was given in the local language (Kinyarwanda) to document name and address, marital status, spouse's profession, and obstetric and transfusion history. Blood (10 ml) was taken for HIV serology and thick drop examination for trophozoites of *P. falciparum*. The remaining serum was frozen for later studies.

All sera were screened for HIV antibodies with a commercial EIA (Wellcome Diagnostics, Research Triangle Park, NC) in the Kigali laboratory of one of the authors (P.V.). A commercial Western blot (Du Pont, Wilmington, DE) was used as a confirmatory test. Western blots were considered positive if they had antibody to a core protein (p17, p25, p55) and antibody to at least one envelope protein (gp41, gp120, gp160). Specimens

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Informed consent was obtained from women participating in the study, which was conducted in accordance with guidelines of the US Department of Health and Human Services and with the approval of the University of California, San Francisco, Committee on Human Research, and the government of Rwanda.

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Table 1. Distribution of human immunodeficiency virus (HIV) infection in Rwandan women by age, marital status, and partner's profession.

	Distribution of women		% with HIV antibodies
	n	%	
Age (years)			
18–20	371	10	31
21–25	1343	36	33
26–30	1296	35	30
31–35	692	19	19
Total	3702	100	29
Marital status			
Legal marriage	1639	44	21
Common law union	1708	46	33
Single/divorced/ widowed/separated	355	10	46
Total	3702	100	29
Partner's profession*			
Farmer	95	4	15
Military	118	5	21
Unemployed	30	1	27
House worker	125	5	28
Civil servant	527	20	29
Private sector	1686	65	30
Other	28	1	—
Total	2609	100	28

NOTE. Values for HIV antibody prevalence by marital status and partner's profession are age-adjusted. Statistical significance was computed by χ^2 for the age subgroup and by the Mantel Haenszel test for marital status and partner's profession subgroups. Differences among age and marital status subgroups in the percentage with antibodies were significant at $P < .001$ and among partner's profession subgroups at $P < .05$.

* Includes cohabiting partners of women in common law unions; 1093 whose partner's professions were not known were excluded. House workers include housekeepers, cooks, and gardeners. "Other" partners (includes students and entrepreneurs) could not be age-adjusted because some age categories were empty.

with only one band were considered negative. Western blot was positive in 95% of EIA-positive sera.

Blood smears were stained with Giemsa and evaluated by a single technician in the pathology laboratory of one of the authors (S.A.). Parasite density was graded as 1+, 2+, or 3+. All positives and an equal number of randomly selected negatives were reviewed blindly by a second technician; disparities were adjudicated by S.A. Thick drop results were available for 90% of the women screened; the remaining 10% were uninterpretable or lost during processing and transport.

Data entry and analysis. Data were entered on site and edited in response to range and logic checks done by the biostatistics staff at the Center for AIDS Prevention Studies in San Francisco. Proportions were age-adjusted to the sample age distribution. χ^2 and χ^2 for trend were used to compare proportions; the Mantel Haenszel χ^2 test was used for age-adjusted proportions.

Results

Demographic distribution of HIV infection. The overall prevalence of HIV antibodies was 29%. The prevalence classified by demographic variables is given in table 1. Because the women were recruited from prenatal and pediatric clinics, they were sexually active and fertile. Most were 21–30 years old, and 90% had a cohabiting sexual partner; one-half of these were in legal marriages.

Women in legal marriages had a substantially lower age-adjusted prevalence of infection (21%) than did those in common law unions (33%), and both were less likely to be infected than those who were single, divorced, widowed, or separated (46%). Women >30 years and those married to farmers and military men had relatively low prevalences of infection.

There was a strong inverse association between number of children and HIV infection, which remained when data were stratified by age and marital status (table 2).

Relationship of HIV infection to history of transfusion. A history of transfusion was reported by 225 (6%) of the women; 40% of these had HIV antibodies (table 3). Over 99% had been transfused in Rwanda; most received blood at the Centre Hospitalier de Kigali. Analysis by date of transfusion showed that blood products were associated with high rates of infection (45%) among those transfused in 1980–1985. Transfusion after 1985 (when screening in Rwanda was instituted by the Red Cross) was accompanied by attenuation of this risk, but the number of recent transfusions is too small for this decline to be statistically significant. Those who were never transfused had a prevalence of infection of 28%.

Relationship of HIV infection to malaria. *P. falciparum* trophozoites were found in 9% of thick drops examined, decreasing over time from 12% in the first 10 weeks of screening (the rainy season) to 6% in the last 10 weeks (the dry season). The prevalence of malaria parasites decreased with age of the women (table 4). The age-adjusted prevalence of malaria in

Table 2. Distribution of human immunodeficiency virus (HIV) infection in Rwandan women by age, marital status, and number of children.

	Legal marriage		Common law union	
Age (years), no. of children	No.	% with HIV antibodies	No.	% with HIV antibodies
21–25				
0–2	342	26	479	41
3–4	133	17	221	30
≥5	24	8	21	33
Total	499	23	721	37
26–30				
0–2	200	30	109	36
3–4	265	23	270	33
≥5	178	17	159	28
Total	643	23	538	32

NOTE. Results are for women aged 21–25 and 26–30 who cohabited with a male partner; numbers in other age categories were too small for analysis. Statistical significance of the differences among subgroups in the percentage was computed by χ^2 for trend. $P < .01$ for all groups, except those 26–30 years in common law unions for which $P = .16$.

Table 3. Distribution of human immunodeficiency virus (HIV) infection in Rwandan women by history of blood transfusion.

Transfusion status	Distribution of women		% with HIV antibodies
	No.	%	
Transfused	225	6.1	40
Before 1980	39	1.0	22
1980–1985	165	4.5	45
1986–1987	21	0.6	30
Never transfused	3477	93.9	28
Total	3702	100	29

NOTE. HIV antibody prevalences are age adjusted. The comparison between the proportion infected who reported ever being transfused (40%) and the proportion infected who reported never being transfused (28%) was statistically significant ($P < .001$ by Mantel Haenszel test). Among those transfused in 1986–1987, the proportion infected did not differ from the proportion infected who were transfused in 1980–1985 ($P = .34$).

the outskirts of town (15%) was twice the prevalence in the city center (8%) ($P < .001$). This is the opposite of the pattern for HIV infection, which was more prevalent in the city center (where the age-adjusted prevalence was 31%) than in the outskirts (20%) ($P < .001$).

Stratification showed no relationship between presence of parasitemia and antibodies to HIV in the whole sample or in either residential area (table 4). Similarly, no relationship was found between degree of parasitemia and the age-adjusted prevalence of HIV infection (table 5).

Discussion

In this consecutive sample of 3702 women presenting to the prenatal and pediatric clinics at the Centre Hospitalier de Kigali, and representative of childbearing women in Kigali, the prevalence of antibodies to HIV was 29%. This percentage is similar to that found among urban women of the same age group in a national serosurvey conducted at about the same time using modified cluster sampling methodology [19, 20].

Table 4. Prevalence of malaria parasites in Rwandan women by age, residential area, and human immunodeficiency virus (HIV) infection.

	No.	% thick-drop positive	*P*
Age (years)			
18–20	337	13	
21–25	1183	10	
26–30	1188	9	<.01
31–35	618	7	
Total	3326	9	
Residential area			
City center, HIV^+	828	8	
HIV^-	1864	8	.99
Total	2692	8	
Outskirts, HIV^+	127	17	
HIV^-	507	14	.37
Total	634	15	

NOTE. Statistical significance of age-specific prevalences was computed by χ^2 for trend. Values for malaria prevalence by residential area were age-adjusted; statistical significance of the differences in age-adjusted prevalences between those with and without HIV antibodies was computed by Mantel Haenszel test.

Table 5. Prevalence of human immunodeficiency virus (HIV) infection in Rwandan women with different levels of malaria parasitemia.

Thick drop result	No.	% with HIV antibodies
Negative	3019	29
Rare trophozoites	100	26
1+	142	34
2+ or 3+	61	30
Total	3326	29

NOTE. Statistical significance of the differences in age-adjusted prevalences computed by Mantel Haenszel test was $P = .47$.

The cellular immune system is an important part of the defense against malaria [28–30], and an increased susceptibility to malaria among those infected with HIV would not be unexpected. Moreover, malaria infection might facilitate infection with HIV as the virus replicates more easily in antigenically stimulated lymphocytes [31]. The results of our cross-sectional study suggest that there is not an important relationship between infection with HIV and the presence or severity of parasitemia, and indicate that the epidemic of HIV is unlikely to increase carriage and transmission rates of malaria substantially. The data are also consistent with different routes of transmission of the two diseases, that is with lack of transmission of HIV by anopheles mosquitos [32].

Because most subjects with severe symptoms of malaria would not have been included in this relatively healthy sample, the results do not rule out the possibility that HIV-infected patients with malaria have a more severe clinical course. Furthermore, repeated infection with malaria may influence the natural history of disease among those infected with HIV. As examples of this latter type of parasite-virus interaction, malaria is believed to act as a cofactor for Epstein-Barr virus–associated Burkitt's lymphoma in Africa [33, 34] and strongyloides or filariae may be cofactors for HTLV-I–induced leukemia [35, 36]. Prospective studies are needed to determine whether repeated immunosuppression or stimulation due to parasite infection hastens progression of HIV disease.

As in other studies, younger women had a higher prevalence of HIV infection [5, 19, 20]. The women in the sample who cohabited with a male sex partner (90%) were at significantly lower risk than single mothers. Among women with cohabiting partners, one-half were in common law unions, and prevalence among these subjects was higher than among legal wives. This result, independent of age, suggests that

common law unions are more often nonmonogamous. Women in legal marriages were at comparatively lower risk, but the prevalence of infection in this group was still noteworthy: At 20%, it is the highest seroprevalence rate reported in a "low-risk group" from this part of Africa.

As previously noted in Rwanda [17], living outside the city was associated with a lower risk of HIV infection. We also found a tendency for women with husbands in the military to have lower infection rates, possibly because many recruits have recently moved to the city from the rural areas or because AIDS education and condoms are provided in the camps.

Several factors may be responsible for the higher risk of HIV infection found in each age group among women who had fewer children. Women infertile due to infection with other venereal disease would be likely to have a higher prevalence of HIV. However, infertility is uncommon among Rwandan women attending prenatal and pediatric clinics, and a more likely interpretation is that the number of children is an indirect measure of the duration or degree of monogamy of a sexual union. It is also possible (though we have no evidence for it) that there may be less sexual intercourse during pregnancy or that the women may be less susceptible to the infection when they are pregnant.

The transfusion findings show that being a recipient of blood contributed to the risk of HIV infection between 1980 and 1985 when seroprevalence in the population was high and blood donor screening for HIV was not yet available. However, transfusions during this period were reported by <5% of the women, so this avenue for spread accounts for only a small fraction of the infection in Rwanda.

This study shows that the Red Cross blood screening campaign in Rwanda can only account for a relatively small number of HIV infections prevented. The high prevalence of infection even in the lowest risk groups of the general population of Kigali highlights the need to develop effective prevention programs for sexual transmission, the pathway believed responsible for the great majority of HIV infections in Rwanda.

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