JAIDS Journal of Acquired Immune Deficiency Syndromes
23:405–409 © 2000 Lippincott Williams & Wilkins, Inc., Philadelphia

High HIV Incidence and Prevalence Among Young Women in Rural South Africa: Developing a Cohort for Intervention Trials

*†David Wilkinson, *S. S. Abdool Karim, ‡Brian Williams, and *Eleanor Gouws

**Centre for Epidemiological Research in South Africa, Medical Research Council, Hlabisa, South Africa; †South Australian Centre for Rural and Remote Health, The University of Adelaide and the University of South Australia, Whyalla and Adelaide, Australia; and ‡Epidemiology Research Unit, Johannesburg, South Africa*

Objective: To measure prevalence and model incidence of HIV infection.

Setting: 2013 consecutive pregnant women attending public sector antenatal clinics in 1997 in Hlabisa health district, South Africa. Historical seroprevalence data, 1992–1995.

Methods: Serum remaining from syphilis testing was tested anonymously for antibodies to HIV to determine seroprevalence. Two models, allowing for differential mortality between HIV-positive and HIV-negative people, were used. The first used serial seroprevalence data to estimate trends in annual incidence. The second, a maximum likelihood model, took account of changing force of infection and age-dependent risk of infection, to estimate age-specific HIV incidence in 1997. Multiple logistic regression provided adjusted odds ratios (OR) for risk factors for prevalent HIV infection.

Results: Estimated annual HIV incidence increased from 4% in 1992/1993 to 10% in 1996/1997. In 1997, highest age-specific incidence was 16% among women aged between 20 and 24 years. In 1997, overall prevalence was 26% (95% confidence interval [CI], 24%–28%) and at 34% was highest among women aged between 20 and 24 years. Young age (<30 years; odds ratio [OR], 2.1; $p = .001$), unmarried status (OR 2.2; $p = .001$) and living in less remote parts of the district (OR 1.5; $p = .002$) were associated with HIV prevalence in univariate analysis. Associations were less strong in multivariate analysis. Partner's migration status was not associated with HIV infection. Substantial heterogeneity of HIV prevalence by clinic was observed (range 17%–31%; test for trend, $p = .001$).

Conclusions: This community is experiencing an explosive HIV epidemic. Young, single women in the more developed parts of the district would form an appropriate cohort to test, and benefit from, interventions such as vaginal microbicides and HIV vaccines.

Key Words: HIV incidence; Rural South Africa; Young women; Intervention trials.

South Africa is experiencing a rapidly progressing HIV epidemic. Annual surveys among pregnant women seen at public prenatal clinics show that HIV prevalence increased nationally from 0.76% in 1990 to 14.07% in 1996 (1). In the east coast province of KwaZulu-Natal, 19.9% of women attending antenatal clinics were infected in 1996. In the rural district of Hlabisa in KwaZulu-Natal, HIV prevalence has been measured in various sentinel groups. Among pregnant women, prevalence increased from 4.2% in 1992 to 14.0% in 1995 (2); of 360 patients presenting with a sexually transmitted disease (STD) in 1997, 43% tested HIV positive (3); and in the same year 65% of 304 adults with tuberculosis were HIV infected (unpublished data).

Address correspondence and reprint requests to David Wilkinson, SACRRH, C/- University of South Australia—Whyalla Campus, Nicolson Avenue, Whyalla Norrie SA 5608, Australia; email: david.wilkinson@unisa.edu.au.

Manuscript received October 16, 1999; accepted January 7, 2000.

Appropriate responses to the HIV epidemic are well documented but at program level they have at best only been partially effective (4). Although awareness of HIV/AIDS in South Africa is high, little evidence suggests sexual behavior has changed, that condom use is high, or that STDs are being effectively treated (5). To develop prevention strategies, a better understanding of the transmission dynamics of HIV infection, including incidence rates, is required. These data are also essential for identifying a cohort appropriate for testing large-scale community-based interventions such as vaginal microbicides and HIV vaccines.

The aim of this study was to measure prevalence and to model incidence of HIV infection among pregnant women seen at public sector antenatal clinics in Hlabisa, South Africa in preparation for large scale, community-based intervention trials.

METHODS

Setting

KwaZulu/Natal, with a population of approximately 9 million, is the largest of South Africa's nine provinces. The population of the largely rural Hlabisa health district is approximately 210,000. Most residents are Zulu-speaking and live in widely scattered homesteads, depending on pensions, migrant labor, and subsistence farming for money and food. A major national road and trading route crosses the district and a large township is situated on this road. The annual per capita income in KwaZulu/Natal is 5189 South African rand (R) (or roughly $1730. in U.S. dollars), the literacy rate 69%, and life expectancy is 63 years.

Prenatal HIV Testing

Prenatal care is provided by the local district hospital, 10 community clinics, and two mobile clinic teams. Approximately 95% of pregnant women in the district receive prenatal care at these clinics (6). At their first antenatal visit, all women have blood taken to test for syphilis infection. For seroprevalence surveys, personal identifiers were removed from the remaining serum, which was stored at 4°C until being frozen at −20°C within 48 hours. Data on the name of the clinic attended, age, marital status, and whether the woman's partner is a migrant worker (defined as spending more nights away than at home) were collected. Results of surveys done in 1992, 1993, and 1995 have previously been reported (2). We could not link sera from previous pregnancies because all surveys were anonymous.

Two different enzyme-linked immunosorbent assay (ELISA) tests were used to screen for anti-HIV antibodies. Specimens negative on the first ELISA (Abbott Axsym: HIV-1, p24 and p41; HIV-2, p36; Abbott Laboratories, Abbott Park, IL, U.S.A.) were reported as negative and not tested further. Specimens positive on the first ELISA were tested with a second ELISA having a different antigen combination (Ominimed UNIFORM II: HIV-1, p24, gp160; HIV-2, env peptide, Organon, Boxtel, The Netherlands). Specimens were reported as positive if both tests were positive; those testing positive on the first ELISA and negative on the second ELISA were subjected to a confirmatory antigen test (Abbott Antigen HIV-1 p24, HIV-1 gp41, HIV-2 gp36). Confidential and voluntary HIV counseling and testing were available for women who requested it following the HIV education course that is a routine part of prenatal care; the number of women who request this is not routinely recorded by the clinics.

Analysis

Serum samples were available from 2013 women seen at prenatal clinics between January and April 1997. For a 2-week period when approximately 350 specimens were collected, demographic data were inadvertently not obtained. Prevalence data have been stratified by age, marital status, partner's status as a migrant worker, and clinic visited. The clinic at which care was sought is a good indication of the woman's place of residence because most women go to the clinic nearest their home and access to care is good (D. Le Sueur, Medical Research Council National Malaria Research Programme, personal communication). Given that many variables are likely to be highly interrelated, a multiple logistic regression model was fitted, and both unadjusted and adjusted odds ratios (OR) are presented. The multiple logistic model contained age group, marital status, partner status, and clinic as well as interaction terms for marital status*partner, marital status*clinic location, partner status*clinic location, and age group*marital status.

Incidence rates were modeled from serial prenatal clinic seroprevalence data (2) using two models. The first was a method for estimating incidence from prevalence data for irreversible diseases adjusting for differential mortality (7), which was used to estimate annual incidence rates between 1992 and 1997. The annual mortality rate among HIV-positive women was assumed to be 10% (8). This model assumes an exponential increase in disease prevalence with age, and inasmuch as age-specific HIV prevalence does not behave this way, it cannot be used to model age-specific incidence rates. A second model was therefore derived, using a generalization that allows for a changing force of infection and for age-dependence of risk of infection (Williams and Gouws, submitted for publication).

This second model is an extension of that described by Gregson et al. (9) who consider the estimation of incidence from age-prevalence data when an epidemic has reached a steady state. Because the prevalence of infection in Hlabisa continues to increase rapidly we have had to extend the model of Gregson et al. to allow for this. To do so, we assume that in the years before the cross-sectional survey was carried out, the overall prevalence was increasing exponentially. Support for this assumption is found in measures of the overall prevalence of infection among prenatal clinic patients in Hlabisa (2) and in the prenatal clinic data for the province of KwaZulu/Natal (1). We then assume that the risk of acquiring disease is determined by the product of the force of infection, which is proportional to the overall prevalence at any time, and an age-risk function, which is determined by the likelihood that people will engage in high risk sex as a function of age. The age-risk function must be zero below a certain age because several datasets for South Africa show that below the age of 15 years, the prevalence of infection among girls is either zero or very low. Among girls, the prevalence of infection increases rapidly and then decreases with age beyond the age of about 25 years. A log-normal function has this general form and we have therefore chosen this to fit the age-risk function. Although age-risk function does not change over time, this does not imply that the shape of the age-incidence function does not change over time as the model is stratified by age. The log-normal function gives a good fit to this, as well as to a wide range of other data sets (Williams et al. manuscript in preparation). An exponential survivorship curve is assumed with a median life expectancy of 7 years, which corresponds to an annual mortality of those with HIV of 10% per year. Maximum likelihood methods were used to fit the model to the prevalence data available for 1997, assuming current HIV prevalence of 26%, an epidemic exponential growth rate of 0.3204 per year, and

annual mortality among HIV-infected women of 10%. This second model was used only to estimate age-specific HIV incidence in 1997.

RESULTS

Prevalence

In 1997, of 2013 consecutive serum samples, 521 (26%; 95% confidence interval [CI], 24%–28%) tested positive for anti-HIV antibodies. The highest age-specific prevalence was 34% among women aged between 20 and 24 years, but a high prevalence (25%) was also observed among young women aged between 15 and 19 years (Table 1).

Information on marital status was available for 1639 women (81%). Prevalence of infection was substantially higher among single women (29%) than either married (16%; $p = .0002$) or engaged to be married women (16%; $p = .01$). The adjusted OR for infection in single women compared with women married or engaged to be married was 2.1 (95% CI, 0.9–-4.8), (Table 2).

Data on partner's status as a migrant worker were available for 1626 women (81%). There was little difference in prevalence of HIV infection among women with a migrant-worker partner (26%), compared with those whose partners were resident (28%), even when adjusted for other variables (OR 0.9; Table 2).

Data on the clinics visited were available for 1564 (78%) women (Table 3) and considerable heterogeneity of HIV prevalence was observed (χ^2 test for trend; $p = .001$). Women seen at clinics that are situated on, or close to larger, paved roads, in more developed parts of the district (clinics 6–9 and 11–13) tended to have higher prevalence (average, 29%). Conversely, women attending clinics situated on or close to smaller, dirt roads, in more remote rural parts of the district (clinics 2–5) had lower prevalence (average, 21%; $p = .001$). Clinics 1 and 10 (Table 3) are mobile clinics serving multiple points across the district and hence are not shown on the map. The clinic with the highest prevalence (clinic 13) serves a large periurban settlement alongside a major national road.

TABLE 1. *Age-specific HIV prevalence and incidence among 1635 women seen at antenatal clinics in Hlabisa, South Africa*

Age group (y)	No. HIV-positive	No. tested	Percent HIV-positive (95% CI)	Incidence[a]
15–19	95	382	25 (21–29)	10
15	2	9	22 (4–56)	
16	6	36	17 (7–31)	—
17	21	96	22 (14–31)	
18	34	135	25 (18–33)	
19	32	106	30 (22–39)	
20–24	169	495	34 (30–38)	16
25–29	98	347	28 (24–33)	12
30–34	50	225	22 (17–28)	7
35–39	12	132	9 (5–15)	4
>40	6	52	12 (5–22)	1

[a] Assumes 10% annual mortality rate among HIV infected women. In all, 1635 (81%) of 2013 samples had the age recorded; 2 specimens were from women below 15 years and have not been included on this analysis.

TABLE 2. *Univariate and multivariate analysis of risk factors for HIV infection*

Risk factor	Proportion HIV-infected	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Age (y)			
<30	30%	32.1 (1.6–2.8)[a]	1.6 (0.9–3.2)
≥30	17%		
Marital status			
Married	16%		
Single	29%	2.2 (1.6–3.1)[a]	2.1 (0.9–4.8)
Partner status			
Resident	28%		
Migrant	26%	0.9 (0.7–1.1)	0.9 (0.4–1.9)
Clinic location			
Smaller road	21%		
Larger road	29%	1.5 (1.2–1.9)[a]	1.7 (0.8–3.4)

[a] $p < .05$

Adjusted odds ratio (OR) and 95% confidence interval (CI) derived from a multiple logistic model containing age group, marital status, partner status, and clinic as well as interaction terms marital status · partner, marital status · clinic, partner status · clinic location, and age group · marital status.

TABLE 3. *Clinic-specific HIV prevalence among 1564 women seen at antenatal clinics in Hlabisa, South Africa*

Clinic	No. HIV-positive	No. tested	Percentage (95% CI) HIV-positive
1	27	156	17 (12–24)[a]
2	18	95	19 (12–28)
3	13	68	19 (11–30)
4	24	105	22 (16–32)
5	26	106	25 (17–33)
6	44	168	26 (20–33)
7	25	93	27 (19–37)
8	75	272	28 (23–33)
9	11	39	28 (16–44)
10	7	24	29 (14–49)
11	11	36	31 (17–47)
12	24	78	31 (21–42)
13	112	363	31 (26–36)[b]

Clinics 1 and 10 are mobile clinics serving multiple points across the district.

Compared prevalence for each clinic with that in the whole district.

1564 (78%) of 2013 samples had the code for the source clinic recorded; clinics 1 and 10 are mobile clinics serving several points throughout the district.

[a] $p = .01$.

[b] $p = .04$.

CI, confidence interval.

Incidence

Estimated age-specific incidence rates of HIV infection in 1997 are shown in Table 1. Assuming 10% differential mortality, among women aged between 15 and 40 years, overall annual HIV incidence was estimated at 10%, and the highest age-specific incidence rate was 16% for women aged between 20 and 24 years. Assuming zero mortality the corresponding rates were 8% and 14%, respectively.

Using historical seroprevalence data (2) in the first model (7), and assuming a 10% mortality rate (8), annual incidence rates for 1992 to 1997 were estimated at 4% (standard error [SE], 1.6) for 1992/1993; 3% (SE, 1.7) for 1993/1994; 5% (SE 1.7) for 1994/1995;, 8% (SE, 1.8) for 1995/1996; and 10% (SE, 2.1) for 1996/1997.

Fitting an exponential curve to the measured seroprevalence data from 1992 to 1995 predicts a prevalence of 36% in 1998.

DISCUSSION

Although the HIV epidemic developed relatively late in South Africa, it is growing rapidly as shown by the dramatic rise in prevalence of HIV infection among women seen at public prenatal clinics. This seems to be consequent on incidence rates that have risen rapidly in recent years and that are currently at very high levels, especially among young, single women. Interventions, such as condom promotion and improved treatment of sexually transmitted diseases, which have been effective in some settings have been difficult to implement and evaluate at program scale in sub-Saharan Africa. New preventive strategies such as vaginal microbicides and HIV vaccines are therefore required and young, single women living in the more developed parts of this district would form an appropriate cohort in whom to test emerging products.

The prevalence of HIV infection reported in this key sentinel surveillance group is among the highest reported from sub-Saharan Africa (10,11). Although there is some debate about how representative pregnant women are of the general female population (12,13), prevalence in this sentinel group may actually underestimate prevalence among women of similar age in the general community because of the apparent association between HIV infection and reduced fertility (12–14). In 1995, ~95% of women in the district went to clinics for prenatal care, and there has been little change in the number of women seen in recent years (6). The very high prevalence rates observed among women aged between 15 and 19 years (Table 2), which are more likely to represent incident cases, provide some external validity to our modelling.

Podgor and Leske (7) describe a method for estimating incidence from age-specific prevalence data for irreversible diseases where mortality risks differ for persons with and without disease. One limitation of applying this method to HIV data is the assumption that disease incidence and population composition remain constant over time. However, when applying this method to our HIV prevalence data, assuming a 10% mortality rate among diseased persons, the overall incidence was estimated to be 9.6%. This is in close agreement with the average incidence estimate of 9.8% when using the generalized model, which allows for changing force of infection. The first model was therefore used to estimate overall annual incidence rates from 1992 to 1997, years for which overall annual prevalence data were available. The second, generalized, model was only applied to the 1997 data for which age-specific prevalences were available, and from which the risk of acquiring infection could be estimated as a function of age. We did this because the assumption made by Podgor and Leske that age-specific disease prevalence increases exponentially does not apply to HIV. A sensitivity analysis with mortality set at 0% resulted in lower estimates of incidence, as expected. However, the differences were small, suggesting that our assumptions concerning mortality associated with HIV are reasonable.

Why is the incidence of HIV infection so high, and the epidemic progressing so rapidly, in much of South Africa? It seems likely that the combination of high levels of STDs and substantial population movement is of major importance. In Hlabisa, it has been estimated that ≈ 25% of all women of reproductive age have at least one STD at any given time, that half these are asymptomatic, and that only 1% to 2% are adequately treated (15). Under these conditions, transmission inevitably continues virtually unchecked. Migration—or population movement—is a substantial risk factor for HIV infection. In one South African study, HIV infection was three times more common in people who had recently changed their place of residence (16), and in another community survey, all HIV infections identified were among the partners of migrant workers (17). Around 90% of households in Hlabisa have at least one man who works away and 60% of school children reported that their father spent most nights away from home (M. Lurie, MRC, personal communication). Many of these men have town families and/or have sex with commercial sex workers when away from home. South Africa's excellent transport infrastructure allows frequent returns home for these migrant workers and the infections that they acquire

while away. We observed substantially higher HIV prevalence among women living in areas on or adjacent to larger roads, but not among women with migrant partners. This implies that in this district, risk for infection is multifactorial and the effect of male migration itself is perhaps less important than the high prevalence of STDs that we have reported (15), or that male migration is qualitatively different in different parts of the district or perhaps for married rather than single women.

We also observed a large difference in HIV prevalence between single and married women, suggesting a substantial change in behavior among women and/or men when they marry. This observation may also reflect some selection of marital partner differential on perceived risk status. Promoting a delay in sexual debut and younger age at marriage may reduce the length of the high-risk period between these key milestones. Some evidence suggests that such changes in sexual behavior have occurred in Uganda recently, with a corresponding fall in HIV prevalence in some areas (18). However, these changes are small (18) and although currently available interventions must be vigorously promoted, new prevention strategies must also be developed. Communities with high HIV incidence rates are likely to benefit most from large scale community-based interventions that employ products such as vaginal microbicides and HIV vaccines. Microbicides may be particularly attractive to the rural partners of male migrant workers because their use can be covert if necessary and thus remains under the woman's control. Candidate vaccines and microbicides with some potential are now emerging, and field sites need to be made ready for phase 2 and phase 3 trials. Young, single women in the more developed parts of this district experience very high HIV incidence rates and hence would form an appropriate cohort to test, and subsequently benefit from, such interventions. Effectiveness of any intervention could be assessed rapidly under these conditions and cohort members would benefit both from any positive effect of the product, as well as the concurrent stronger efforts at promotion of condom use and safer sex practices.

REFERENCES

1. Department of Health. Sixth national HIV survey of women attending antenatal clinics of the public health services in the Republic of South Africa, October 1995. *Epidemiol Comments* 1996; 23:3–17.
2. Coleman R, Wilkinson D. Increasing HIV prevalence in a rural district of South Africa. *J Acquir Immune Defic Syndr Hum Retrovirol* 1997;16:50–3.
3. Wilkinson D, Wilkinson N. HIV infection among patients with sexually transmitted diseases in rural South Africa. *Int J STD AIDS* 1998;9:736–9.
4. UNAIDS. The status and trends of the global HIV/AIDS pandemic symposium final report. Vancouver, 5–6 July 1996. AIDSCAP/ Family Health International, Harvard School of Public Health, UNAIDS.
5. Directorate: HIV/AIDS and STD. *National STD/HIV/AIDS review.* Pretoria, SA: Department of Health, 1998.
6. Wilkinson D, Cutts F, Ntuli N, Abdool Karim SS. Maternal and child health indicators in a rural South African health district. *S Afr Med J* 1997;87:456–9.
7. Podgor MJ, Leske MC. Estimating incidence from age-specific prevalence for irreversible diseases with differential mortality. *Stat Med* 1986;5:573–8.
8. Nunn AJ, Mulder DW, Kamali A, Ruberantwari A, Kengeya-Kayondo J, Whitworth J. Mortality associated with HIV-1 infection over five years in a rural Ugandan population: cohort study. *BMJ* 1997;315:767–71.
9. Gregson S, Donnelly CA, Parker CG, Anderson RM. Demographic approaches to the estimation of incidence of HIV-1 infection among adults from age-specific prevalence data in stable endemic conditions. *AIDS* 1996;10;1689–97.
10. US Bureau of the Census. *HIV/AIDS in Africa.* Research note no. 20. Washington, DC: Health Studies Branch, International Programs Center, Population Division, U.S. Bureau for the Census, 1996.
11. US Bureau of the Census. *HIV/AIDS surveillance database.* Washington, DC: Population Division, International Programs Center, Population Division, U.S. Bureau for the Census, 1997.
12. Batter V, Matela B, Nsuami M, et al. High HIV-1 incidence in young women masked by stable overall seroprevalence among childbearing women in Kinshasha, Zaire: estimating incidence from serial seroprevalence data. *AIDS* 1994;8:811–7.
13. Biosson E, Nicoll A, Zaba B, Rodrigues LC. Interpreting HIV seroprevalence data from pregnant women. *AIDS* 1996;13:434–9.
14. Gray RH, Wawer MJ, Serwadda D, et al. Population-based study of fertility in women with HIV-1 infection in Uganda. *Lancet* 1998;351:98–103.
15. Wilkinson D, Abdool Karim SS, Harrison A, et al. Unrecognised sexually transmitted infections in rural South African women—the hidden epidemic. *Bull WHO* 1998;9:548–50.
16. Abdool Karim Q, Abdool Karim SS, Singh S, Short R, Ngxongo S. Seroprevalence of HIV infection in rural South Africa. *AIDS* 1992; 6:1535–9.
17. Colvin M, Abdool Karim SS, Wilkinson D. Migration and AIDS. *Lancet* 1995;46:1303.
18. Mulder D, Nunn A, Kamali A, Kengeya-Kayondo J. Decreasing HIV-1 seroprevalence in young adults in a rural Ugandan cohort. *BMJ* 1995;311:833–6.