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Ecological and individual level analysis of risk factors for HIV infection in four urban populations in sub-Saharan Africa with different levels of HIV infection

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<ABS> **Objective:** To identify factors that could explain differences in rate of spread of HIV between different regions in sub-Saharan Africa.

<ABS> **Design:** Cross-sectional study.

<ABS> **Methods:** The study took place in two cities with a relatively low HIV prevalence (Cotonou, Benin and Yaoundé, Cameroon), and two cities with a high HIV prevalence (Kisumu, Kenya and Ndola, Zambia). In each of these cities, a representative sample was taken of about 1000 men and 1000 women aged 15–49 years. Consenting men and women were interviewed about their socio-demographic background and sexual behaviour; and were tested for HIV, herpes simplex virus type 2 (HSV-2), syphilis, *Chlamydia trachomatis* and *Neisseria gonorrhoea* infection, and (women only) *Trichomonas vaginalis*. Analysis of risk factors for HIV infection was carried out for each city and each sex separately. Adjusted odds ratios (aOR) were obtained by multivariate logistic regression.

<ABS> **Results:** The prevalence of HIV infection in sexually active men was 3.9% in Cotonou, 4.4% in Yaoundé, 21.1% in Kisumu, and 25.4% in Ndola. For women, the corresponding figures were 4.0, 8.4, 31.6 and 35.1%. High-risk sexual behaviour was not more common in the high HIV prevalence cities than in the low HIV prevalence cities, but HSV-2 infection and lack of circumcision were consistently more prevalent in the high HIV prevalence cities than in the low HIV prevalence cities. In multivariate analysis, the association between HIV infection and sexual behavioural factors was variable across the four cities. Syphilis was associated with HIV infection in Ndola in men [aOR = 2.7, 95% confidence interval (CI) = 1.5–4.9] and in women (aOR = 1.7, 95% CI = 1.1–2.6). HSV-2 infection was strongly associated with HIV infection in all four cities and in both sexes (aOR ranging between 4.4 and 8.0). Circumcision had a strong protective effect against the acquisition of HIV by men in Kisumu (aOR = 0.25, 95% CI = 0.12–0.52). In Ndola, no association was found between circumcision and HIV infection but sample sizes were too small to fully adjust for confounding.

<ABS> **Conclusion:** The strong association between HIV and HSV-2 and male circumcision, and the distribution of the risk factors, led us to conclude that differences in efficiency of HIV transmission as mediated by biological factors outweigh differences in sexual behaviour in explaining the variation in rate of spread of HIV between the four cities.

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<KWS> **Keywords: HIV, sub-Saharan Africa, cross-sectional study, male circumcision, herpes simplex virus type 2, risk factors, HIV spread, ecological study, sexually transmitted infections, sexual behaviour**

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Introduction

By the end of the year 2000, an estimated 36.1 million people were living with HIV worldwide [1]. Of these, 70% were living in sub-Saharan Africa, which houses about 10% of the world's population. It has been estimated that 8.8% of adults in sub-Saharan Africa are infected with HIV and that 90% of these infections are acquired through sexual intercourse between men and women. However, the burden of the HIV/AIDS epidemic is not equally distributed over the continent: the prevalence of HIV infection is generally higher in East and South Africa than in West and Central Africa [2]. The general objective of the multicentre study on factors determining the differential spread of HIV in four African cities was to identify factors that could explain differences in prevalence of HIV infection between different regions in sub-Saharan Africa. The study was conducted in two cities with a high HIV prevalence (Kisumu, Kenya and Ndola, Zambia) and two cities with a relatively low HIV prevalence (Cotonou, Benin and Yaoundé, Cameroon). There is evidence that the differences in prevalence between these four cities are due to differences in rate of spread of HIV, rather than to differences in time since the start of the HIV epidemics [3].

Numerous studies have been conducted in sub-Saharan Africa on risk factors for HIV infection. These risk factors can be grouped into two categories, including sexual behavioural risk factors [4–9] and factors that influence the transmission of HIV during sexual intercourse [10]. The latter factors include, among others, classical sexually transmitted infections (STIs) [11], male circumcision [12], condom use and certain sexual practices, such as anal intercourse and possibly also 'dry sex' [10].

This paper first presents a comparison between the four cities of the distribution of factors that have been found in other studies to be risk factors for HIV infection, or that are believed to be associated with an increased risk of HIV. Following this, the association between these risk factors and HIV infection is explored at the individual level in men and women in the four cities. Factors found to be associated with an increased risk of HIV infection at the individual level and more prevalent in the two high HIV prevalence cities than in the two low HIV prevalence cities are likely to play a major role in explaining the differences in HIV prevalence between the four cities.

Methods

The methods of the data collection and laboratory procedures are described in detail elsewhere and only a summary is given here [3]. In each of the four cities, a survey was conducted in the general population and among a random sample of sex workers. The surveys took place between June 1997 and March 1998. The aim was to collect data on a representative sample of 1000 men and 1000 women aged 15–49 years from the general population in each city. Households were selected by two-stage random sampling, and all eligible men and women in the selected households were asked to participate in the study. After giving their informed verbal consent, study participants were interviewed about their socio-demographic characteristics and sexual behaviour, using a standardized questionnaire [13]. The questionnaire on sexual behaviour included a section on characteristics of the spouse and of the non-spousal partnerships of the past 12 months (to a maximum of eight). Men were also interviewed about past and present symptoms suggestive of a STI and about their health-seeking behaviour. After the interview, study participants were asked to give a blood sample, which was tested for HIV, syphilis and herpes simplex virus type 2 (HSV-2), and a urine sample, which was tested for *Neisseria gonorrhoea* and *Chlamydia trachomatis* infection. Women were asked to insert a swab into the vagina, which was immediately inoculated into a culture medium for *Trichomonas vaginalis*.

Statistical analysis

All data were double-entered and validated in EPI-INFO version 6.04a (CDC, Atlanta, Georgia, USA). Further data cleaning and data analysis was carried out with SPSS version 8.0 for Windows (SPSS, Inc., Chicago, Illinois, USA) and SAS (version 6.12; Cary, North Carolina, USA).

The analyses presented in this paper were restricted to men and women who reported that they had ever had sexual intercourse. In each of the four cities. almost all HIV infections were in respondents who reported sexual activity [14].

Variables

The socio-demographic variables examined included: age; educational attainment; having a job, as opposed to not having a job; having made more than one trip out of the city in the past 12 months; religion (Catholic, Protestant, Muslim or other); ethnic group; and alcohol consumption in the past month. In men, circumcision was also explored as a potential risk factor for HIV infection. Men were categorized as being circumcised on the basis of the clinical examination, but if no clinical examination was performed they were categorized as circumcised if they reported this in the interview.

The sexual behaviour characteristics that were explored as potential risk factors for HIV infection included: marital status, age at first sexual intercourse, residence in the city at age of first sex, lifetime number of sex partners, number of non-spousal partners in the past 12 months, one or more short-term partnerships (of less than 1 months duration) in the past 12 months, and sex in exchange for money. In men, contact with a female sex

PAF has been estimated for the acquisition of HIV and does not take into account increased transmission of HIV by dually HIV/HSV-2-infected individuals.

Figure 1 shows a tentative qualitative synthesis of the driving forces behind the HIV epidemics in men. In this simplified model, sexual activity leads to the spread of HIV and HSV-2. Male circumcision reduces the transmission efficiency of HIV and possibly also HSV-2. HSV-2 increases the transmission efficiency of HIV, and HIV increases the transmission efficiency of HSV-2. In this 'male circumcision–HSV-2' model of HIV spread, HSV-2 and HIV have a mutually positive feedback, and male circumcision has a negative feedback on HIV transmission and possibly HSV-2 transmission. This simplified model suggests that: (i) without a high prevalence of male circumcision, the mutual activation of HIV and HSV-2 leads to a rapid spread of both infections even if sexual activity is not particularly high; (ii) with a high prevalence of male circumcision, HIV and HSV-2 spread remains relatively limited; and (iii) with a high prevalence of male circumcision, HIV could only spread relatively widely if HSV-2 reaches high levels as a result, for example, of high levels of sexual activity. This could explain the relatively low HIV prevalence in Yaoundé. The high prevalence of HIV in Kisumu and Ndola is mainly due to HSV-2 infection in a non-circumcising population.

It is not within the scope of this paper to discuss in detail the implications of our findings for prevention strategies. However, some general and preliminary conclusions can be drawn. Male circumcision should be considered a prevention strategy in non-circumcising populations that are heavily affected by the HIV epidemic, as has been suggested previously [36]. Because HIV is likely to be transmitted between spouses, voluntary HIV testing and counselling, particularly before marriage, should be encouraged — provided it remains truly 'voluntary'. So far, there are no specific tools for the prevention of HSV-2 infection. Suppressive therapy as a prevention strategy for HSV-2 infection is not feasible in sub-Saharan Africa, considering the high prevalence of HSV-2. The development of a vaccine against the infection or a therapeutic vaccine is needed and trials with it should include HIV infection as an endpoint. In the meantime, prevention of HSV-2 infection has to rely on the promotion of safe sex; in particular, condom use.

References

1. UNAIDS & World Health Organization. *AIDS Epidemic Update: December 2000*. Geneva: UNAIDS and WHO; 2000.
2. UNAIDS. **Report on the global HIV/AIDS epidemic. *UNAIDS/00.13E*.** Geneva: UNAIDS; June 2000.
3. Buvé A, Caraël M, Hayes RJ, *et al.* **Multicentre study on factors determining differences in rate of spread of HIV in sub-Saharan Africa: methods and prevalence of HIV infection**. *AIDS* 2001, **15 (suppl 4)**:S5–S14.
4. Bassett MT, McFarland WC, Ray S, Mbizvo MT, Machekano R, van de Wijgert JH, Katzenstein DA. **Risk factors for HIV infection at enrollment in an urban male factory cohort in Harare, Zimbabwe**. *J Acquir Immune Defic Syndr Hum Retrovirol* 1996, **13**:287–293.
5. Chao A, Bulterys M, Musanganire F, *et al.* **Risk factors associated with prevalent HIV-1 infection among pregnant women in Rwanda. National University of Rwanda–Johns Hopkins University AIDS Research Team**. *Int J Epidemiol* 1994, **23**:371–380.
6. Gomo E, Chibatamoto PP, Chandiwana SK, Sabeta CT. **Risk factors for HIV infection in a rural cohort in Zimbabwe: a pilot study**. *Cent Afr J Med* 1997, **43**:350–354.
7. Malamba SS, Wagner H-U, Maude G, *et al.* **Risk factors for HIV-1 infection in adults in a rural Ugandan community: a case–control study**. *AIDS* 1994, **8**:253–257.
8. Nunn AJ, Kengeya-Kayondo JF, Malamba SS, Seeley JA, Mulder DW. **Risk factors for HIV-1 infection in adults in a rural Ugandan community: a population study**. *AIDS* 1994, **8**:81–86.
9. Quigley M, Munguti K, Grosskurth H, *et al.* **Sexual behaviour patterns and other risk factors for HIV infection in rural Tanzania: a case–control study**. *AIDS* 1997, **11**:237–248.
10. Buvé A, Caraël M, Hayes R, Robinson NJ. **Variations in HIV prevalence between urban areas in sub-Saharan Africa: do we understand them?** AIDS 1995, **9 (suppl A)**:S103–S109.
11. Fleming DT, Wasserheit JN. **From epidemiological synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection**. *Sex Transm Inf* 1999, **75**:3–17.
12. Weiss HA, Quigley MA, Hayes RJ. **Male circumcision and risk of HIV infection in sub-Saharan Africa: a systematic review and meta-analysis**. *AIDS* 2000, **14**:2361–2370.
13. UNAIDS. **Looking deeper into the HIV epidemic: a questionnaire for tracing sexual networks**. In *Best Practice Collection, Key Material 98/27*. Geneva: UNAIDS; 1998:1–24.
14. Buvé A, Lagarde E, Caraël M, *et al.* **Interpreting sexual behaviour data: validity issues in the multicentre study on factors determining the differential spread of HIV in four African cities**. *AIDS* 2001, **15 (suppl 4)**:S117–S126.
15. Bruzzi, P, Green SB, Byar DP, Brinton LA, Schairer C. **Estimating the population attributable risk for multiple risk factors using case–control data**. *Am J Epidemiol* 1985, **122**:904–914.
16. Thompson ML, Myers JE, Kriebel D. **Prevalence odds ratio or prevalence ratio in the analysis of cross sectional data: what is to be done?** *Occup Environ Med* 1998, **55**:272–277.
17. Skov T, Deddens J, Petersen MR, Endahl L. **Prevalence proportion ratios: estimation and hypothesis testing**. *Int J Epidemiol* 1998, **27**:91–95.
18. Auvert B, Buvé A, Lagarde E, *et al.* **Male circumcision and HIV infection in four cities in sub-Saharan Africa**. *AIDS* 2001, **15 (suppl 4)**:S31–S40.
19. Caraël M, Van De Perre Ph, Lepage Ph, *et al.* **Immunodeficiency virus transmission among heterosexual couples in Central Africa**. *AIDS* 1988, **2**:201–205.
20. Serwadda D, Wawer MJ, Musgrave SD, Sewankambo NK, Kaplan JE, Gray RH. **HIV risk factors in three geographic strata of rural Rakai District, Uganda**. *AIDS* 1992, **6**:983–989.
21. Bwayo J, Plummer F, Omari M, *et al.* **Human immunodeficiency virus infection in long-distance truck drivers in east Africa**. *Arch Intern Med* 1994, **154**:1391–1396.
22. Simonsen JN, Cameron DW, Gakinya MN, *et al.* **Human immunodeficiency virus infection among men with sexually transmitted diseases. Experience from a center in Africa**. *N Engl J Med* 1988, **319**:274–278.
23. Morison L, Weiss HA, Buvé A, *et al.* **Commercial sex and the spread of HIV in four cities in sub-Saharan Africa**. *AIDS* 2001, **15 (suppl 4)**:S61–S69.
24. Boily M-C, Anderson RM. **Sexual contact patterns between men and women and the spread of HIV-1 in urban centres in Africa**. *IMA J Math Appl Med Biol* 1991, **8**:221–247.
25. Glynn JR, Caraël M, Auvert B, *et al.* **Why do young women have a much higher prevalence of HIV than young men? A study in Kisumu, Kenya and Ndola, Zambia**. *AIDS* 2001, **15 (suppl 4)**: S51–S60.
26. Gregson S, Nyamukapa C, Mason P, Garnett G, Zhuwau T, Anderson R, Chandiwana S. **Population-based survey of HIV infection and its socio-demographic and behavioural determinants in rural Manicaland, Zimbabwe, 1998–1999**. Presented at the *XIII International AIDS Conference*, Durban, South Africa, 9-14 July 2000 [abstract TuPeC3447].