

## Genital Ulcers Associated with Human Immunodeficiency Virus–Related Immunosuppression in Female Sex Workers in Abidjan, Ivory Coast

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A cross-sectional study among female sex workers in Abidjan was conducted to study the association between sexually transmitted diseases and human immunodeficiency virus (HIV) infection and HIV-related immunosuppression. Among 1209 women tested for HIV, 962 (80%) were seropositive. HIV infection was independently associated with a longer duration of sex work, a lower price for intercourse, being an immigrant, and having a positive *Treponema pallidum* hemagglutination test ( $P < .05$ ). Genital ulcers (25% vs. 5%), genital warts (14% vs. 4%), *Neisseria gonorrhoeae* (32% vs. 16%), *Trichomonas vaginalis* (27% vs. 17%), and syphilis (27% vs. 17%) were more frequent ( $P < .05$ ) in HIV-infected than -uninfected women. Among HIV-infected women, the proportions with a genital ulcer were 17%, 25%, and 36% for those with  $>28\%$ , 14%–28%, and  $<14\%$  CD4 cells, respectively ( $P < .001$ ). This study suggests that genital ulcers are an opportunistic disease in female sex workers in Abidjan.

In sub-Saharan Africa, female sex workers and their clients appear to play a primary role in the dynamics of the human immunodeficiency virus (HIV) epidemic [1]. In Abidjan, the overall HIV seroprevalence among female sex workers increased from 38% in 1987 to 69% in 1990 [2]. Sexually transmitted diseases (STDs) facilitate the transmission of HIV [3]. Whether HIV-related immunosuppression affects the acquisition, pathogenicity, or natural history of certain STDs is also a critical research issue. The present study sought to determine the prevalence of HIV infections and STDs among female sex workers in Abidjan, to identify risk factors for HIV infection,

and to study the association between STDs and HIV infection and HIV-related immunosuppression in this population.

### Methods

A cross-sectional study was conducted from October 1992 through April 1994 at a clinic for female sex workers. Sex workers were contacted at their places of work through an education program of the Institut National de Santé Publique of the Ivory Coast Ministry of Health [4] and invited to come to the clinic. Each was administered a standard questionnaire and given general and gynecologic examinations. The following syndromes were diagnosed clinically: Bartholinitis, genital ulcer disease, genital warts, and pelvic inflammatory disease (presence of  $\geq 2$  of the following signs: lower abdominal tenderness, adnexal tenderness, cervical motion tenderness, and cervical mucopurulent discharge).

A wet mount preparation of vaginal secretions collected from the posterior vaginal fornix was examined for the presence of *Trichomonas vaginalis*. *Chlamydia trachomatis* was detected by EIA (Syva, Dardilly, France). Material from an endocervical swab was plated on site onto modified Thayer-Martin medium and incubated in a candle extinction jar at 36°C for 24–48 h. *Neisseria gonorrhoeae* was identified presumptively by Gram's stain and demonstration of oxidase [5].

Beginning in January 1993, material was swabbed from the base of genital ulcers and cultured for *Haemophilus ducreyi* on enriched gonococcal agar and Mueller-Hinton medium [5]. After incubation at 34°C for 48–96 h in a candle extinction jar, *H. ducreyi* was presumptively identified on the basis of its characteristic colony morphology and Gram's stain results. From October 1992 through September 1993, material from a second swab was taken to Antwerp in virus transport medium and cultured in Vero cells for herpes simplex virus (HSV).

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Informed consent was obtained from all study participants. The study was approved by the Ethical Committee, Ivory Coast Ministry of Health.

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Venous blood was obtained for HIV and syphilis serology and for hematology. Sera were tested for antibodies to HIV-1 and -2 by an algorithm that included a whole-virus ELISA (Genetic Systems, Seattle) or a mixed-antigen ELISA (Genelavia-mixt; Diagnostics Pasteur, Paris), a synthetic peptide-based test (Pepti-LAV; Diagnostics Pasteur) and Western blot (New-LAV blot; Diagnostics Pasteur, and HIV blot 2.2; Diagnostic Biotechnology, Geneva), as described [6]. Specific antitreponemal antibodies were detected by *Treponema pallidum* hemagglutination assay (TPHA; Fujirebio, Tokyo); a rapid plasma reagin (RPR) test was also done (Macro-Vue; Becton Dickinson, Erembodegem, Belgium). A woman was considered to have syphilis when both TPHA and RPR tests were positive. Flow cytometry (FACscan; Becton Dickinson) was used for lymphocyte subset typing and counting, and total lymphocyte count was done by automated blood analyzer (Coulter Counter; Coultronics, Margency, France). CD4 percentages (<14%, 14%–28%, and >28%) were used to classify women as having severe, moderate, or minimal immunosuppression, respectively [7].

Any STD detected was treated without charge on the day of enrollment and the subject was given a supply of condoms. Laboratory test results, posttest counseling for HIV/AIDS, and additional treatment, if indicated, were given during a second visit 1 week after enrollment.

Data were analyzed by Epi-Info (CDC) and SPSS (SPSS, Chicago) statistical packages. The 95% confidence intervals (CIs) and the odds ratio (OR) were calculated by parametric or exact methods. Univariate significance tests used Yates's corrected  $2 \times 2 \chi^2$  test or Fisher's exact test for dichotomous variables and the  $\chi^2$  test for linear trend for ordered categorical variables. In the analysis of risk factors for HIV infection, the TPHA test was used as a surrogate marker for past high-risk sexual behavior. Logistic regression was done using models that included all factors that were associated in the univariate analysis. Significance ( $P < .05$ ) was based on Wald's test.

## Results

The 1281 participating women had a mean age of 29 years, were largely immigrants (84%) and uneducated (47%), and had worked a mean of 4 years. They received a mean of 1113 francs from their last client (\$1 = 300 francs for most of the study period). Condoms were used during 50% of 4838 reported sexual contacts.

A total of 1209 women (94%) agreed to HIV testing. The overall HIV prevalence was 80%; 567 (47%) were HIV-1 seropositive, 31 (3%) were HIV-2 seropositive, and 364 (30%) reacted to both HIV-1 and -2. In the univariate analysis, HIV infection was associated with older age, being an immigrant, longer duration of sex work, lower price for intercourse, having a positive TPHA, having a higher number of unprotected sexual contacts during the last work day, having no other occupation, and having sex during menses (table 1). In a logistic regression model, HIV infection remained independently associated with being an immigrant, a longer duration of sex work, a lower price for intercourse, and a positive TPHA.

The prevalences of STDs and syndromes in this population were as follows: gonorrhoea (29%), trichomoniasis (25%),

**Table 1.** Potential risk factors for HIV infection in female sex workers in Abidjan, Ivory Coast.

	HIV-positive no. (%)	Adjusted odds ratio (95% confidence interval)*
Age (years)		
<20	96/137 (70)	NS
20–29	398/506 (79)	
30–39	341/412 (83)	
≥40	124/150 (83)	
Immigrant		
No	118/201 (59)	1.0
Yes	844/1008 (84)	2.4 (1.7–3.5)
School education		
No	470/579 (81)	
Yes	490/628 (78)	NI
Duration of sex work (months)		
1–12	249/348 (72)	1.0
13–24	169/215 (79)	1.4 (0.9–2.1)
25–60	277/337 (82)	1.6 (1.1–2.4)
>60	266/308 (86)	2.0 (1.3–3.3)
Price for intercourse (francs) <sup>†</sup>		
≥2000	125/224 (56)	1.0
1000–1999	276/347 (80)	3.0 (2.0–4.4)
500–999	319/367 (87)	3.9 (2.5–6.0)
<500	241/270 (89)	4.8 (2.9–8.1)
<i>Treponema pallidum</i> hemagglutination test		
Negative	571/748 (76)	1.0
Positive	389/459 (85)	1.4 (1.0–2.0)
No. of clients not using condoms (last work day)		
0	198/270 (73)	NS
1	222/287 (77)	
2	256/310 (83)	
≥3	285/341 (84)	
Other occupation		
No	770/950 (81)	
Yes	190/257 (74)	NS
Oral contraceptives		
No	930/1162 (80)	NI
Yes	29/43 (67)	
Anal sex		
Never	927/1160 (80)	NI
Ever	34/47 (72)	
Sex during menses		
No	605/781 (78)	NS
Yes	354/423 (84)	

\* Derived from logistic regression model with all factors significantly associated in univariate analysis; NS, not significant ( $P > .05$ ); NI, not associated in univariate analysis ( $P > .05$ , Yates's corrected  $2 \times 2 \chi^2$  or test for linear trend  $\chi^2$ ) and therefore not included in model.

<sup>†</sup> For most of study, 300 francs = \$1 (US).

syphilis (25%), genital ulcer (21%), pelvic inflammatory disease (12%), genital warts (11%), chlamydial infection (5%), and Bartholinitis (3%). The STDs and syndromes found significantly more frequently in HIV-positive than -negative women were genital ulcers (25% vs. 5%; OR, 6.0; 95% CI, 3.4–10.7), genital warts (14% vs. 4%; OR, 4.1; 95% CI, 2.0–

**Table 2.** Prevalence of sexually transmitted diseases (STDs) by level of immunosuppression in HIV-infected female sex workers in Abidjan, Ivory Coast.

STD	Prevalence, (%)			P*
	<14% CD4 cells	14%–28% CD4 cells	>28% CD4 cells	
Genital ulcer	65/180 (36)	126/497 (25)	44/258 (17)	<.001
+ <i>Haemophilus ducreyi</i> <sup>†</sup>	9/36 (25)	27/67 (40)	5/26 (19)	NS
+ Herpes simplex virus <sup>‡</sup>	5/37 (14)	12/82 (15)	4/28 (14)	NS
Undetermined <sup>§</sup>	13/18 (72)	21/36 (58)	11/19 (58)	NS
Localization <sup>  </sup>				
Cervix	19/64 (30)	13/126 (10)	4/42 (10)	.001
Vagina	32/64 (50)	62/126 (50)	12/42 (29)	.05
Vulva	35/64 (55)	84/126 (67)	35/43 (81)	.004
Perineum	7/64 (11)	15/126 (12)	5/43 (12)	NS
<i>Trichomonas vaginalis</i>	68/180 (38)	131/500 (26)	55/256 (22)	<.001
Syphilis	42/180 (23)	126/502 (25)	82/258 (32)	.04
Genital warts	27/175 (15)	72/478 (15)	23/247 (9)	.05
Bartholinitis	10/179 (6)	14/500 (3)	6/258 (2)	NS
<i>Neisseria gonorrhoeae</i>	44/171 (26)	175/489 (36)	79/252 (31)	NS

\* Value of  $\chi^2$  test for linear trend; NS, not significant ( $P > .05$ ).

<sup>†</sup> From January 1993, denominator is no. of women with genital ulcer; no culture was done for 7, 8, and 0 women with <14%, 14%–28%, and >28% CD4 cells, respectively.

<sup>‡</sup> From October 1992 through September 1994, denominator is no. of women with genital ulcer; no culture was done for 13, 20, and 12 women with <14%, 14%–28%, and >28% CD4 cells, respectively.

<sup>§</sup> From January 1993 through September 1994, denominator is no. of women with genital ulcer for whom both cultures (*H. ducreyi* and herpes simplex virus) were done.

<sup>||</sup> Denominator is no. of women with genital ulcer; multiple genital ulcers may have >1 localization.

8.1), *N. gonorrhoeae* (32% vs. 16%; OR, 2.6; 95% CI, 1.8–3.8), *T. vaginalis* (27% vs. 17%; OR, 1.8; 95% CI, 1.3–2.7), and syphilis (27% vs. 17%; OR, 1.7; 95% CI, 1.2–2.4). While bartholinitis was more frequent in HIV-positive than -negative women, the difference was of borderline significance (3% vs. 1%; OR, 3.9; 95% CI, 1.0–34.2). No significant difference was observed between HIV-positive and -negative women for chlamydial cervicitis (5% vs. 5%) or pelvic inflammatory disease (11% vs. 14%).

Among 940 HIV-seropositive women, 180 (19%) had severe, 502 (53%) had moderate, and 258 (27%) had minimal immunosuppression. Table 2 shows the prevalences of STDs that were associated with HIV infection by level of immunosuppression in HIV-positive women. A strong linear trend with immunosuppression was observed for genital ulcers. This trend remained significant when controlling for other factors that were associated in the univariate analysis (no education, low price for intercourse, and young age).

The prevalence of chancroid was 8%, 9%, and 3% in HIV-positive women with <14%, 14%–28%, and >28% CD4 cells respectively ( $P = .04$ ,  $\chi^2$  for linear trend). The prevalence of genital herpes was 4%, 3%, and 2% in HIV-positive women with <14%, 14%–28%, and >28% CD4 cells, respectively ( $P > .05$ ,  $\chi^2$  for linear trend). The proportion of neither chancroid nor herpes among ulcer cases was associated with immunosuppression levels in HIV-positive women (table 2). With increasing immunosuppression, genital ulcers were less fre-

quently localized on the vulva but found more frequently on the cervix (table 2).

*T. vaginalis* was also strongly associated with immunosuppression levels in HIV-positive women. Weak trends were observed for genital warts (increasing prevalence) and syphilis (decreasing prevalence), while there was no significant trend for *N. gonorrhoeae* or bartholinitis.

## Discussion

The association detected in this study between genital ulcers and HIV-related immunosuppression suggests that genital ulcers are an opportunistic disease in female sex workers. In the absence of effective preventive behavior, transmission of HIV from these sex workers may be enhanced by both immunosuppression and genital ulcers [8–11].

HIV infection was independently associated with being an immigrant, longer duration of sex work, lower price for intercourse, and a positive TPHA. Caution is needed when interpreting these “independent” associations, as it is impossible to adequately control for sexual exposure in a cross-sectional study. While longer duration of sex work and a positive TPHA are expected risk determinants and possibly true causal factors, the interpretation of the association between HIV infection and being an immigrant and lower price for intercourse is less straightforward. They may in fact be markers for a variety of risk factors that increase the women’s exposure or susceptibility

to HIV infection, such as an increased number of clients, higher prevalences of HIV or other STDs among the clients, or lower condom use rates.

Genital ulcers, *N. gonorrhoeae*, genital warts, syphilis, and *T. vaginalis* were all significantly more frequent among HIV-infected women. However, these associations do not necessarily reflect causal relationships, as both HIV infection and the associated STD may be caused by a common etiologic factor (i.e., sexual exposure). Thus, we examined whether there was an association between these STDs and the severity of immunosuppression in HIV-positive women.

Genital ulcers were independently associated with increasing immunosuppression among HIV-positive women. While sexual exposure may not have been fully controlled for, it is unlikely that this association was caused by increased sexual exposure in women with more severe immunosuppression, as one would then expect an increased frequency of all STDs. In a study in Nairobi, Kenya, genital ulcers were more frequent in female sex workers with clinical signs of immunosuppression [8]; the present study confirms this relationship on the basis of laboratory evidence of immunosuppression.

The prevalence of chancroid tended to be higher in HIV-positive women with moderate or severe immunosuppression. However, the proportion of *H. ducreyi* culture-positive ulcers among all cases of genital ulcer was not associated with the severity of immunosuppression. If chancroid is indeed more frequent in immunosuppressed women, the association may be explained by HIV-related immunosuppression, which facilitates the acquisition or development of chancroid or prolongs its course with [12] or without treatment. Unexpectedly, herpetic genital ulcers were not significantly more frequent with increasing immunosuppression. It may be that genital herpes is an opportunistic disease only in patients with extreme immunosuppression [13]. No etiology could be determined in a considerable proportion of genital ulcers. This can partly be explained because *H. ducreyi* is difficult to grow (the sensitivity of culture is estimated to be 60%–70% in optimal conditions [14]) and by a probable loss of sensitivity of HSV cultures due to transport. It also is possible that a considerable proportion of genital ulcers in women with severe immunosuppression is due to causes other than HSV and *H. ducreyi*.

Genital ulcers were more often located on the cervix in women with severe immunosuppression. Thus, these ulcers may be overlooked when no speculum examination is done. The cervical localization of genital ulcers in immunosuppressed women may also facilitate transmission of HIV from these women.

The observed association of *T. vaginalis* with immunosuppression has not been described previously and will need to be confirmed.

In conclusion, intervention programs in this population are needed to promote effective preventive behavior, to lower prevalences of STDs in general and genital ulcers in particular, and to provide care for women with HIV infection. Since this study showed that genital ulcers are more frequent in HIV-related immunosuppression, it is likely that control of genital ulcers is more

difficult in populations with high prevalences of HIV. Further research should be conducted into the etiology and response to treatment of genital ulcers in HIV-infected populations.

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