

# Prostitution, HIV, and Cervical Neoplasia: A Survey in Spain and Colombia<sup>1</sup>

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## Abstract

**The prevalence of cervical intraepithelial neoplasia (CIN) and the association of CIN with prostitution was examined in Oviedo, a region in Spain with low incidence of cervical cancer, and in Cali, Colombia, where the incidence of cervical cancer is 6–10 times higher. In Oviedo, the study included 758 prostitutes attending a sexually transmitted diseases clinic and 1203 nonprostitutes attending a family-planning clinic. In Cali, 775 prostitutes and 1795 nonprostitutes attending health centers were included. Seropositivity to common sexually transmitted agents was investigated in Spanish prostitutes.**

**No significant difference was found in the prevalence of CIN between Oviedo and Cali in both prostitutes (2.5 versus 1.8%) and nonprostitutes (1.2 versus 1.1%). Prostitutes had a 2-fold increased risk of CIN as compared to nonprostitutes; in Spain, the prevalence odds ratio (POR) was 2.3 and the 95% confidence interval (CI) was 1.1–4.5, and, in Colombia, POR was 1.8 and the 95% CI was 0.9–3.5. Among prostitutes in Oviedo, human immunodeficiency virus (HIV) prevalence was 4.9% and HIV-positive prostitutes showed a high risk of CIN as compared to HIV-negative prostitutes (POR, 12.7; 95% CI, 3.9–40.9); 76% of HIV-positive prostitutes were i.v. drug users and showed an increased seroprevalence of other sexually transmitted diseases. HIV-negative prostitutes did not show any increased risk of CIN (POR, 1.2; 95% CI, 0.5–2.8).**

**These results show that among nonprostitutes the prevalence of CIN was not statistically different between the two cities in Spain and Colombia; prostitutes were at moderate increased risk compared to nonprostitutes in both cities. HIV-positive prostitutes were at an increased risk for CIN. These findings are consistent with the hypothesis that HIV infection, irrespective of the route of exposure, increases the risk of acquiring**

**human papillomavirus and/or enhances the expression of human papillomavirus infection as CIN.**

## Introduction

One of the features of the occurrence of cervical cancer is its marked geographical variation, an example of which is the 6–10-fold higher incidence rates reported in Colombia as compared to Spain (1, 2). A few specific types of HPV<sup>2</sup> have been proposed as etiological agents (3) and recognized as key risk factors of cervical cancer in epidemiological studies (4, 5) and multidisciplinary reviews (6, 7). It has been suggested that the geographical variation in the incidence of cervical cancer could be related to the patterns of sexual behavior of the populations and particularly to the use of prostitutes by men (8).

Prostitutes are recognized as a high-risk group for all STDs, including infections with HPV and HIV, but only a few studies have reported high risks for CIN and cervical cancer (9–11).

As part of a series on studies of risk factors and geographical differences in the incidence of cervical cancer, we have undertaken a survey of CIN among prostitutes in the cities of Cali in Colombia and Oviedo in the northern part of Spain. The reported age-adjusted incidence rates of cervical cancer were 48.2/100,000 in 1977–1981 in Cali and 7.4/100,000 in 1984 in Oviedo (1, 2). Incidence data for the period 1977–1981 are available for areas in Spain close to the Oviedo region and confirm the consistent low rates in the country (1).

## Subjects and Methods

In 1990–1991 the medical records and cytological reports from several medical institutions providing services to prostitutes in Oviedo and Cali were reviewed.

In Oviedo, the survey included 758 prostitutes attending an STD clinic at the Hospital Monte Naranco during the period 1985–1990, as well as the records of 1203 nonprostitutes attending a family-planning clinic in the same hospital. The information systematically collected included date of first visit, age, place of birth, previous history of CIN, duration of practicing prostitution, and the cytological results from cervical smears. For prostitutes, information was also available on the use of i.v. drugs only for those that were HIV positive. Exposure to STA was assessed as follows: antibodies to *Treponema pallidum* (fluorescent treponemal an-

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<sup>2</sup> The abbreviations used are: HPV, human papillomavirus; CIN, cervical intraepithelial neoplasia; STA, sexually transmitted agent; STD(s), sexually transmitted disease(s); HIV, human immunodeficiency virus; POR, prevalence odds ratio; CI, confidence intervals; AIDS, acquired immunodeficiency syndrome.

Table 1 Number and age distribution of all women included in the surveys and of the cases of CIN<sup>a</sup>

	Oviedo		Cali	
	No. of prostitutes	No. of nonprostitutes	Prostitutes	Nonprostitutes
All women	758 (100)	1182 (100)	775 (100)	1795 (100)
Age groups (yr)				
<20	86 (11.4)	115 (9.7)	55 (7.1)	89 (5.0)
20–29	451 (59.4)	606 (51.3)	402 (51.9)	662 (36.8)
>29	221 (29.2)	461 (39.0)	318 (41.0)	1044 (58.2)
Mean age	26.9 [6.6]	27.9 [6.7]	28.1 [7.3]	33.8 [12.7]
CIN cases	19	14	14	19
Age groups (yr)				
<20	1 (5.3)	0 (0)	1 (7.1)	1 (5.3)
20–29	13 (68.4)	3 (21.4)	5 (35.7)	8 (42.1)
>29	5 (26.3)	11 (78.6)	8 (57.2)	10 (52.6)
Mean age	26.8 [4.5]	35.1 [7.9]	28.1 [6.6]	31.6 [11.8]

<sup>a</sup> Numbers in parentheses, percentages; numbers in brackets, SD.

tibody absorbance); *Chlamydia trachomatis* (immunofluorescence) as previously described (12); HIV (enzyme-linked immunosorbent assay and confirmation with Western blot), and hepatitis B surface antigen (enzyme-linked immunosorbent assay). These assays were performed routinely for prostitutes and only when clinically required for other women attending the clinic. All cytological smears were classified as CIN grades by a reference laboratory, blind to the practice of prostitution. Twenty-one subjects had no information on cytology and were excluded from the analysis.

In Cali, two health centers known to provide gynecological surveillance to women practicing prostitution as well as to the general population were selected (Centro Obrero and Belalcazar). The records of women attending these health centers for the first time during 1985–1989 were reviewed. Information was available on date of first visit, age, practice ever of prostitution, and diagnosis on cytological smears. All cytological smears from these two centers were processed and read at the same laboratory, blind to whether a woman was a prostitute. Slides were initially reported following the Pap classification system and recoded by the same cytopathologists to CIN grades for consistency with the Spanish results. A total of 775 women reported themselves as prostitutes and 1795 as nonprostitutes and were included in the survey. Of the total number of women in the records, 145 were excluded because no information on cytology was available.

Age-adjusted PORs with 95% CI were computed using unconditional linear logistic regression to estimate the risk of CIN among prostitutes in relation to nonprostitutes.

## Results

Table 1 shows the number of subjects included in the survey by age, prostitution practice, and presence of cervical neoplasia. The population in Oviedo was younger than the population in Cali (mean ages, 27.5 versus 32.1 years,  $P < 0.05$ ). Prostitutes in both countries were younger than their reference group and the difference was of borderline statistical significance in Cali (mean age for prostitutes, 28.1 versus 33.8 years for nonprostitutes;  $P = 0.05$ ). Women with CIN were on average of the same age in both countries (mean age, 30.3 versus 30.1 years).

Table 2 shows the prevalences of CIN in the different groups. The prevalence of CIN did not differ between

Oviedo and Cali among nonprostitutes (1.2 versus 1.1%) or among prostitutes (2.5 versus 1.8%;  $P = 0.4$ ); this could not be explained by differences in the age distribution in each population. In Spain, 15.3% of HIV-positive prostitutes had CIN, whereas only 1.4% CIN cases were identified among HIV negatives ( $P < 0.0001$ ). If the subgroup of HIV positives are excluded, there was no difference in the prevalence of CIN between prostitutes and nonprostitutes (1.2 versus 1.4%). Nonprostitutes with CIN in Cali were more likely to have CIN I than were nonprostitutes in Oviedo (78.9 versus 42.9%;  $P = 0.03$ ) although two cases of invasive cervical cancer were diagnosed among nonprostitutes in Cali and none in Oviedo. Prostitutes in Oviedo, especially HIV-positive ones, were more likely to have CIN I lesions than were prostitutes in Cali, but none of the differences was statistically significant.

Table 3 presents the age-adjusted PORs of CIN among prostitutes in relation to nonprostitutes. In both countries combined, prostitutes were at a 2-fold increased age and country-adjusted risk of CIN (POR, 2.0; 95% CI, 1.2–3.3), but this was statistically significant only in Spain (POR, 2.3; 95% CI, 1.1–4.5). In Oviedo, there was information on the HIV status of 673 prostitutes. The prevalence of seropositivity was 4.9% and no women had clinically overt AIDS at the time. Nonprostitutes were not systematically tested for HIV, but based on estimated population rates of HIV and AIDS, less than one case would be expected (13). If nonprostitutes are taken as reference, the risk of cervical neoplasia for HIV-positive prostitutes could be measured by a POR of 14.2 (95% CI, 4.8–42.4) and there was no increased risk of CIN among HIV-negatives [POR, 1.2; 95% CI, (0.5–2.8)]. Within the group of 673 prostitutes tested, HIV-positive prostitutes showed a very high risk of CIN as compared to HIV-negative prostitutes (POR, 12.7; 95% CI, 3.9–40.9).

Table 4 shows an analysis restricted to 288 prostitutes with serological markers of exposure to at least one of the following STAs: HIV; *C. trachomatis*; *T. pallidum* and hepatitis B surface antigen by HIV status. HIV-positive prostitutes had a greater load of STAs; 36.4% had antibodies to at least two STAs as compared to 11.4% among HIV-negatives ( $P < 0.01$ ).

Fig. 1 shows the prevalence of CIN in prostitutes by seroprevalence to each one of the three most common

Table 2 Prevalence and relative distribution of cervical neoplasia grades as diagnosed among prostitutes and nonprostitutes in Oviedo and Cali<sup>a</sup>

	CIN I	CIN II-III	Invasive	CIN I-III <sup>b</sup> /Total
<b>Oviedo</b>				
Nonprostitutes	6 [42.9]	8 [57.1]	0 [0.0]	14/1182 (1.2)
All prostitutes	13 [68.4]	6 [31.6]	0 [0.0]	19/758 (2.5)
Prostitutes, HIV-positive	4 [80.0]	1 [20.0]	0 [0.0]	5/33 (15.2)
Prostitutes, HIV-negative	6 [66.7]	3 [33.3]	0 [0.0]	9/640 (1.4)
Prostitutes, HIV-unknown	3 [60.0]	2 [40.0]	0 [0.0]	5/85 (5.9)
<b>Cali</b>				
Nonprostitutes	15 [78.9]	4 [21.1]	2 [10.5]	19/1795 (1.1)
Prostitutes	9 [64.3]	5 [35.7]	1 [7.1]	14/775 (1.8)

<sup>a</sup> Numbers in brackets, relative distribution of cases by grade; numbers in parentheses, prevalence of cervical lesions.

<sup>b</sup> Includes invasive cancer cases.

Table 3 POR of cervical neoplasia among prostitutes and nonprostitutes in Oviedo and Cali<sup>a</sup>

	CIN/total (%)	POR (95% CI) <sup>a</sup>
<b>Oviedo</b>		
Nonprostitutes	14/1182 (1.2)	1.0
Prostitutes	19/758 (2.5)	2.3 (1.1–4.5)
HIV-negative	9/640 (1.4)	1.2 (0.5–2.8)
HIV-positive	5/33 (15.3)	14.2 (4.8–42.4)
<b>Cali</b>		
Nonprostitutes	19/1795 (1.1)	1.0
Prostitutes	14/775 (1.8)	1.8 (0.9–3.5)
<b>Total</b>		
Nonprostitutes	33/2977 (1.1)	1.0
Prostitutes	33/1533 (2.1)	2.0 (1.2–3.3) <sup>b</sup>

<sup>a</sup> POR adjusted for age.

<sup>b</sup> POR, adjusted for age and country.

Table 4 Prevalence of antibodies to either HIV, *C. trachomatis*, hepatitis B surface antigen, or *T. pallidum* by HIV status among prostitutes in Oviedo (Spain)

	HIV	
	Positive (%)	Negative (%)
Antibodies to 1 STA	21 (63.6) <sup>a</sup>	226 (88.6)
Antibodies to 2 STAs	10 (30.3)	28 (11.0)
Antibodies to 3 STAs	2 (6.1)	1 (0.4)
All	33 (100)	255 (100)

<sup>a</sup> positive to HIV only.

sexually transmitted agents. Although seropositive prostitutes for either *C. trachomatis* or *T. pallidum* were more likely to have a higher prevalence of CIN, no statistical difference was found between seropositives and seronegatives. HIV-positive prostitutes showed a prevalence of cervical neoplasia significantly higher than those who were HIV-negative (15.2 versus 1.4%;  $P < 0.001$ ).

The risk for CIN among prostitutes in Oviedo was not related to the duration of the practice of prostitution (data not shown).

## Discussion

**CIN among Prostitutes.** The results of our survey indicate that women practicing prostitution were at a 2-fold in-

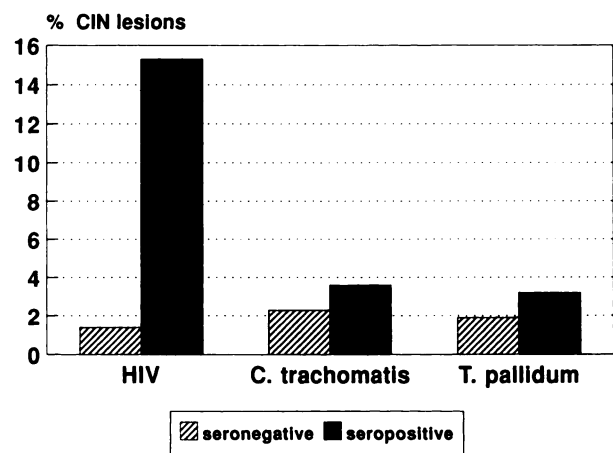


Fig. 1. Prevalence of cervical intraepithelial neoplasia among prostitutes in Oviedo, Spain, with and without antibodies to three STAs.

creased risk for CIN as compared to nonprostitutes. The magnitude of the risk estimate was similar in Oviedo and Cali. In two case-control studies carried out in Cali and Spain, women reporting ever having practiced prostitution showed an almost 3-fold increase risk for CIN III (14). Most of the cases in our survey were CIN I, and, therefore, the moderate increased risk observed for prostitution makes our results consistent with other studies that have described CIN I lesions as epidemiologically different from CIN II and III (15) and perhaps showing a different natural history (16).

**CIN and HIV among Prostitutes.** In Oviedo the association between CIN and HIV among prostitutes was very strong, unlikely to be explained by uncontrolled confounding factors. Spain is one of the European countries with highest rates of AIDS (6.6/100,000 males and females) (13), and both AIDS and HIV positivity are closely related to i.v. drug abuse, especially among women under 30 years of age (17–19). HIV-positive prostitutes in our study were younger than HIV-negative ones and 76% of them were i.v. drug users. Drug addicts have been described as less prone to use preventive measures in relation to HIV and have frequent sexual contacts with men who are themselves drug-users (17). The increased load of sexually transmitted infections among HIV-positive prostitutes described in Table 4 further indicates that HIV positivity among prostitutes is a powerful marker of other STDs and, in our study, also of CIN. It is likely that the

majority of prostitutes in Oviedo were exposed to HIV through i.v. drug use. Our results would suggest that the very high risk of CIN among HIV-positive prostitutes is independent of the route of HIV exposure.

Lack of data on HPV status in our study population prevents us from drawing any conclusion on whether the risk of CIN among HIV-positive women is mediated by HPV infection. However, there are grounds in the literature to suggest that this is the case. There is a strong association between HPV and CIN III in HIV-negative populations in Spain and Colombia (20). Several reports have shown an association between HIV, HPV, and intraepithelial neoplasia in the mucosa of the genital tract (9, 21–29). In the female population of Spain, HIV positivity is a marker of both high-risk sexual behavior and of drug addiction and might result to be a close surrogate of exposure to HPV. In our study populations, CINs were largely grade I, which is morphologically indistinguishable from HPV infection (30). The association found between HIV and CIN may reflect an increased risk for HPV infection among HIV-positive women. It is also consistent with an increased risk for progression from HPV infection to CIN among HIV-positive women. Rapid progression of HPV-induced neoplastic lesions, CIN or anal intraepithelial lesions, has been reported among HIV-positive subjects (23, 24, 29) and more markedly among those with proven immunodeficiency (22, 25, 27, 31). No mechanism for such an interaction has yet been established and it would be of interest to further investigate the strength and consistency of the association between HIV, HPV, and CIN. The potential synergism between the two viruses has been recently addressed by a proposal to include in the definition of AIDS cases, HIV-seropositive women who develop invasive cervical cancer (32).

HIV tests were not systematically done in our study population in Cali. Several estimates indicate that the prevalence of HIV and AIDS (2.0/100,000 males and females (13) are lower in Colombia than in Spain. A survey conducted in 1988 among 1066 prostitutes attending the two health centers included in this study showed an HIV seroprevalence of 0.2% (33) consistent with the unexpected low prevalence of CIN among prostitutes in Cali.

**CIN among Nonprostitutes.** One of the purposes of conducting this survey in Oviedo and Cali was to attempt to explain the geographical differences in the incidence of cervical cancer. The age-adjusted prevalence of CIN I-III among nonprostitutes was similar in the two cities and CIN lesions grade I were more often found in Cali than in Oviedo. Both observations are contrary to expectation in view of the higher incidence of cervical cancer in Colombia. Three main reasons could explain this lack of correlation. Firstly, this could be a spurious finding because this survey was based on existing medical records; no systematic recording of information enabled us to adjust our comparison for likely confounders, notably measures of sexual behavior, rates of participation in screening practices, or differences in socioeconomic level. Secondly, differences in the criteria for CIN diagnosis might occur between Oviedo and Cali; however, results from a concurrent study on cytohistological diagnosis of CIN by a panel of three pathologists from Spain and Cali showed no major differences in the diagnostic criteria for CIN (data not published). Thirdly, these findings could be interpreted as reflecting the effect of a higher prevalence in Cali of agents that act by increasing the progression rate from CIN to invasive carcinoma.

In conclusion, no difference was found in the prevalence of CIN among nonprostitutes in Oviedo and Cali. Prostitution conveyed a moderated increase in risk of CIN compared to nonprostitutes in both cities. In Oviedo, HIV largely accounted for the risk associated to prostitution. These results are consistent with the hypothesis that HIV infection, irrespective of the route of exposure, increases the risk of acquiring HPV and/or enhances the expression of HPV as CIN.

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