

## SHORT REPORT

## Prevalence and risk factors of sexually transmitted infections and cervical neoplasia in women's health clinics in Nicaragua

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*Sex Transm Infect* 2002;**78**:204–207

**Objectives:** To determine prevalence and risk factors of sexually transmitted infections (STIs), HIV, and cervical neoplasia in women attending women's health clinics in Nicaragua, and to assess the potential impact of screening for these diseases.

**Methods:** Consecutive women attending women's health clinics in different regions were interviewed and examined for STI, HIV, and cervical neoplasia.

**Results:** Whereas only 30.4% of the 1185 participating women attended the clinics because of STI related complaints, 77.0% reported symptoms after probing. Clinical cervicitis was diagnosed in 32.8%, *Chlamydia trachomatis* in 4.1%, gonorrhoea in 0.4%, trichomoniasis in 10.2%. Antibodies for syphilis were found in 0.7%, for hepatitis B in 3.7%, and none were HIV seropositive. The STI prevalence was 21.8% in women attending with complaints, 17.3% in symptomatic women after probing, and 14.8% in asymptomatic women. Abnormal Papanicolaou (Pap) smears were found in 7.7%, with high risk human papilloma virus (HPV) types in almost 60%. Male promiscuity was associated with high grade squamous intraepithelial lesions (HSIL) and reported former screening was not shown to be protective. Young age and being employed were risk factors for *C trachomatis*.

**Conclusion:** Nearly one out of five women attending women's health clinics in Nicaragua had an STI, and one out of 13 a precancerous lesion of the cervix. These clinics provide an opportunity to improve the reproductive health of women by probing for STI symptoms, especially in young women, and by offering cervical screening to casual attendees. Of concern is the high rate of cervical lesions in women with a screening history, underlining the need for proper quality control.

In developing countries, sexually transmitted infections (STIs) and HIV are endemic and cervical cancer prevalence high. It has been suggested that integrating STI management and early detection of cervical dysplasia in broader reproductive health services can improve women's health.<sup>1</sup> In Nicaragua, these services are offered in the health centres through the so called "consulta integral a la mujer." Little is known on the burden of disease of women attending this programme. In this study, we wanted to assess the prevalence and risk factors of STI, HIV, and cervical neoplasia in this population and evaluate the potential impact of screening for STI and cervical cancer.

## MATERIAL AND METHODS

## Study population and data collection

From April 1999 to May 2000, sexually active women of all ages, attending the women's health programme in the public

health centres of three districts (capital Managua, the southern district Rivas, and the northern district Matagalpa) and in one centre of the national health service in Managua were invited to participate in the study. Consecutive women attending the consultation were included after giving verbal consent. History was taken, a gynaecological examination was done, samples for laboratory analysis and for Papanicolaou (Pap) smears were obtained.

Blood sera were tested for syphilis using the Macro-Vue RPR Card Test (Becton Dickinson, MD, USA). Reactive sera were diluted and quantified. A rapid plasma reagin (RPR) test  $\geq 1/4$  was considered indicative for syphilis. Testing for HIV-1 and HIV-2 was done by a third generation enzyme immunoassay (EIA) Plus (Abbott, Abbott Park, USA); positive tests were confirmed by western blot assay. An enzyme linked immunosorbent assay (ELISA) test (Human, Wiesbaden, Germany) was used to detect antibodies to hepatitis B virus core antigen (anti-HBc) and a second generation radioimmunoassay (LSU-ICMRT Version 2) to detect hepatitis B surface antigen (HbsAg) for establishing active infections.

*Trichomonas vaginalis* and candida species were diagnosed either on wet mount or by Gram stain. Bacterial vaginosis (BV) was diagnosed using the Nugent score.<sup>2</sup>

Cervical samples were obtained for Gram staining and culture of *Neisseria gonorrhoeae* in Thayer-Martin medium (Merck, Darmstadt, Germany) and in chocolate blood agar medium (Difco, Detroit, MI, USA). Polymerase chain reaction (PCR) (Amplicor, Roche Diagnostics, Ontario, Canada) was used for the detection of *Chlamydia trachomatis* at the Ghent University.

PCR tests for *N gonorrhoeae* were done to confirm gonorrhoea in women with a Gram stain suggestive of intracellular diplococci and a negative culture, as well as in 80 randomly chosen, negative samples. Patients were considered as having gonorrhoea if either the culture or PCR was positive. Human papilloma virus (HPV) detection was done on endocervical swabs of women with an abnormal Pap smear. Samples identified as HPV positive were genotyped with the Inno-Lipa HPV prototype research assay (DDL, Delft, Netherlands), as described previously.<sup>3</sup> HPV amplimers, which do not hybridise to any probe, were assigned HPV genotype X. According to their oncogenic potential, HPV viruses were classified as high or low risk.<sup>4</sup> Pap smears were read using the Bethesda classification.

Patients were asked to return for the laboratory results after 2 weeks. All women with a clinical or laboratory diagnosis

**Abbreviations:** ASCUS, atypical squamous cells of undetermined significance; BV, bacterial vaginosis; EIA, enzyme immunoassay; ELISA, enzyme linked immunosorbent assay; HPV, human papilloma virus; HSIL, high grade squamous intraepithelial lesions; LSIL, low grade squamous intraepithelial lesions; PID, pelvic inflammatory disease; Pap, Papanicolaou; PCR, polymerase chain reaction; RPR, rapid plasma reagin; STIs, sexually transmitted infections

**Table 1** Clinical diagnosis and laboratory results

	Total population (n=1185) (%)	STI related complaints (n=360) (%)	Symptoms after probing (n=552) (%)	Asymptomatic (n=273) (%)
<b>Clinical examination</b>				
Normal	380 (32.1)	89 (24.7)	148 (26.8)	143 (52.4)
GUD	4 (0.3)	2 (0.6)	2 (0.4)	0 (0)
Condylomata	14 (1.2)	9 (2.5)	4 (0.7)	1 (0.4)
Vaginitis	593 (50.1)	195 (54.2)	299 (54.2)	99 (36.4)
Cervicitis	389 (32.8)	129 (35.8)	200 (36.2)	60 (22.0)
PID	76 (6.4)	38 (10.6)	38 (6.9)	0 (0)
<b>Laboratory</b>				
<b>STI</b>				
<i>T vaginalis</i>	119/1175 (10.1)	41/357 (11.5)	55/547 (10.2)	23/271 (8.5)
<i>C trachomatis</i>	40/969 (4.1)	16/292 (5.5)	21/461 (4.6)	3/216 (1.4)
<i>N gonorrhoeae</i>	5/1162 (0.4)	3/354 (0.8)	2/544 (0.4)	0/264 (0)
GUD	4/1180 (0.3)	2/359 (0.6)	2/554 (0.4)	0/267 (0)
Condylomata	14/1184 (1.2)	9/360 (2.5)	4/552 (0.7)	1/272 (0.4)
HIV antibodies	0/1158 (0)	0/356 (0)	0/540 (0)	0/262 (0)
HbsAg	4/1180 (0.3)	1/359 (0.3)	1/549 (0.2)	2/272 (0.7)
HBc antibodies	43/1177 (3.7)	15/358 (4.2)	14/549 (2.6)	14/270 (5.2)
RPR $\geq$ 1/4	8/1185 (0.7)	5/360 (1.4)	3/552 (0.5)	0/273 (0)
At least one STI	213/1175 (18.5)	78/357 (21.8)	95/548 (17.3)	40/270 (14.8)
<b>Non-STI RTI</b>				
<i>Candida</i> species	224/1175 (19.1)	74/357 (20.7)	107/547 (19.6)	43/271 (15.9)
Bacterial vaginosis	359/1176 (30.5)	132/358 (36.9)	155/547 (28.3)	72/271 (26.6)

suggestive of an STI or with cervical dysplasia were counselled and treated free of charge.

#### Data analysis

The data were entered in EPI-INFO (version 6.0) and analysed using SPSS version 10 for Windows (SPSS, Inc, Chicago, IL, USA). Univariate analysis was done using Pearson's  $\chi^2$  test, odds ratio, and 95% confidence intervals (CI) and/or Fischer's exact test and multivariate analysis using the logistic regression (enter model).

## RESULTS

### Demographic data

A total of 1185 women were included in the study, of whom 80% lived in urban areas and 81.0% were married. The mean age was 32.3 years (range 13–72) and 47.3% were housewives. The monthly family income was less than \$US 125 in 69.3% of the families.

### Sexual, reproductive, and screening history

The mean parity was 3.3 and 22% had had at least one abortion. Sexual relations started at a mean of 17.9 years (range 8–35). Only 2.1% reported more than one partner in the last 3 months, but 46% believed their husband or boyfriend had extramarital sex. More than 16% had ever used condoms, in 2.8% on a regular basis and in 1.6% for contraceptive purposes.

Seventy six per cent of women had a Pap test done in lifetime and 47% within the last 3 years. Only 1.2% reported a history of an abnormal Pap result.

### STI related symptoms, signs, and prevalence

Women attended the clinic for a variety of reasons, including 360 (30.4%) for STI related complaints, 67 (5.7%) for pregnancy control, 272 (23.0%) for family planning, and 486 (40.7%) for regular check ups including Pap smear taking. After probing for STI related symptoms, 552 (67.0%) of the women attending for other reasons, admitted having problems. The most reported symptoms were vaginal discharge (58.1%), abdominal pain (35.1%), pruritus (27.7%), and dyspareunia (19.8%). They had duration of less than 1 week in only 7.2%; dyspareunia and abdominal pain were the longest supported symptoms. Previous treatment with antibiotics was reported in 13.5%. A clinical diagnosis of cervicitis and of pelvic inflammatory disease (PID) was made in, respectively,

32.8% and 6.4% of the women. More than 18% of the patients had an STI, though no HIV was detected. An additional 35.7% of women had a non-STI reproductive tract infection, including candidiasis (19.1%) and bacterial vaginosis (30.5%). *T vaginalis* was commonly associated with other pathogens, in 43% with BV, and in 10% with *C albicans*. An overview of clinical and laboratory diagnosis is given in table 1.

### Cervical neoplasia and HPV

Ninety (7.7%) patients had an abnormal Pap result, including 40 (3.4%) atypical squamous cells of undetermined significance (ASCUS), 35 (3.0%) low grade squamous intraepithelial lesions (LSIL), 12 (1.0%) high grade squamous intraepithelial lesions (HSIL), and three (0.3%) invasive cancer. Of those, only 31 (34.4%) came to the clinic for Pap smear taking. All patients diagnosed with invasive cancer attended the clinic for screening reasons, but 75% HSIL were diagnosed in casual attenders. Of the 15 patients with a HSIL or invasive cancer, 13 (86.6%) were previously screened, six of them within the past 12 months and six within the past 3 years. None of them reported an abnormal result on their last Pap smear.

HPV tests were done on 72 patients with abnormal Pap smears (table 2). High risk HPV were present in 54.6% of ASCUS lesions, 62.0% of LSIL and 70.0% of HSIL. Multiple infections were found in 19 (26.4%) patients. One patient with an LSIL was infected with seven different types and another with six. High risk HPV types related to HPV 16 were most prevalent in any of the lesions.

### Determinants of STI and cervical neoplasia

In univariate analysis, age <30 years, being single, being employed, pregnancy, and STI related symptoms were associated with *C trachomatis* infection. No significant associations were found with number of partners, age at first sexual relations, reason for attending the clinic, duration of symptoms, and clinical diagnosis of cervicitis. In multivariate analysis, age <30, being employed and having STI related symptoms remained significant, with adjusted odds ratios (AOR) of 5.2 (95% CI 2.2 to 12.0), 2.4 (95% CI 1.1 to 5.0), and 3.3 (95% CI 1.0 to 10.9) respectively. Fifty per cent of *C trachomatis* cases could be found in the group of symptomatic, employed women younger than 30 years old. In this group, the prevalence was 11.3%.

**Table 2** HPV types

Pap	HPV types				
	No HPV detected	Single infections		Multiple infections	
		No (%)	Low risk or not specified HPV	High risk HPV	Only low risk HPV
ASCUS (n=33)	10 (30.3)	4 (12.1)	12 (36.4)	1 (3.0)	6 (18.2)
LSIL (n=29)	4 (13.8)	7 (24.1)	9 (31.0)	0 (0)	9 (31.0)
HSIL (n=10)	2 (20.0)	1 (10.0)	4 (40.0)	0 (0)	3 (30.0)
Total (n=72)	16 (22.2)	12 (16.7)	25 (34.7)	1 (1.4)	18 (25.0)

Low risk HPV: 6, 11, 34, 40, 42, 43, 44, 53, 54, 70, 74.  
High risk HPV: 16, 18, 31, 33, 39, 45, 51, 52, 56, 58, 59, 66, 68.

Genital ulcers and/or warts were associated with past condom use: AOR 4.1 (95% CI 1.4 to 11.8).

In univariate analysis, HSIL or invasive cancer on current Pap smear was associated with age  $\geq 30$  years (OR 3.35, 95% CI 0.94 to 11.94), having more than three children (OR 5.0, 95% CI 1.6 to 15.8), and reporting non-monogamous partners (OR 11.9, 95% CI 1.5 to 93.4). In multivariate analysis, only the latter remained significant with an AOR of 11.3 (95% CI 1.4 to 82.0). Reporting a normal Pap smear within the past 3 years was not shown to be protective (OR 2.5, 95% CI 0.7 to 8.8).

## DISCUSSION

In this study population, none of the patients was infected with HIV. This is in line with the UNAIDS estimated prevalence rate of 0.1% in Nicaraguan women.<sup>5</sup> However, our data show that the potential for an HIV epidemic exists. Nearly one out of five of this low to middle class, low risk population was found to have an STI. The prevalence of genital ulcer disease and of gonorrhoea was low in our group whereas the prevalence of *C trachomatis* was 4.1% and of *T vaginalis* 10.1%. Condom use was very low, though half of the women believed that their husband or boyfriend had extramarital sex. Even if women might have few possibilities to negotiate sexual and reproductive practices, appropriate health education could increase the reported condom use among women, as shown in a HIV/AIDS programme set up in Managua in 1991–2.<sup>6</sup>

A high prevalence of abnormal smears was found in this population, mainly mild lesions. In women with ASCUS lesions, HPV testing has been suggested as a triage to identify those women most at risk of having an underlying HSIL. In many low resource countries this test is not as widely available as to allow common use. In our study we detected high risk HPV types in more than 50% of ASCUS lesions, indicating that, in the absence of HPV testing, ASCUS lesions should always be further investigated.

As shown in other studies,<sup>7</sup> only a few classic risk factors were significantly associated with genital infections. This might be explained by the importance of male risk behaviour, which is not addressed in this survey. The prevalence of *C trachomatis* in women younger than 30 years is nearly six times higher than in older women. Similar data were found in a study of 863 clinic attendees in three regions in Nicaragua.<sup>8</sup> The higher prevalence in working women could be due to a more liberal sexual behaviour in this group. This was not confirmed by the reported sexual history but, within the culture of machismo, it might be difficult for a woman to mention the number of sexual partners.<sup>9</sup> Another possibility is that these women do have more promiscuous partners.

Genital ulcer disease and genital warts were significant associated with past condom use. We found similar results in studies from Kenya and Azerbaijan.<sup>7, 10</sup> However, other researchers showed that consistent condom use significantly reduced the risk of acquiring genital warts.<sup>11</sup> This might indicate that in our studied populations, condom use is irregular

or that condoms are a surrogate for more risky sexual behaviour, either by the woman or by her partner.

Probably as a result of the small number of cases, the classic risk factors for HSIL and cervical cancer could not be found in our study, with the exception of promiscuous male behaviour. Contrary to what is widely accepted, previous screening was not shown to have a protective effect in this population. The poor quality of Pap smears might be the main reason for this. Whereas it has been mentioned that screening programmes in Latin America should have a wider coverage in order to reduce cervical cancer in these countries,<sup>12</sup> this should be preceded by measures to guarantee the quality of the screening if results are to be reached.

As half of the HSIL and invasive cancers were detected in casual clinic attendees, our data further show the importance of inviting these women to the programme, especially if they are more than 30 years old. On the same line, health providers should ask women for STI related symptoms, and pay special attention to the possibility of *C trachomatis* infections in young women. If the quality of the services were further guaranteed, these simple measures would contribute to more comprehensive care in women's health clinics. To have a substantial impact on women's health, it is necessary to link these clinics with referral level where diagnostic procedures such as colposcopy and biopsy and outpatient treatment of dysplastic lesions can be provided. The district hospital or larger health centres might be excellent sites to provide this care.

## ACKNOWLEDGEMENTS

The authors thank the staff of the health centres and clinics involved in the study, whose collaboration made this work possible.

This study was supported by the Belgian Development Co-operation through the Flemish Interuniversity Council.

## CONTRIBUTORS

PC, study design, analysis of results, manuscript writing; CG, recruitment and examination of patients, clinical advice, and contributions to the manuscript; MG, day to day supervision of the work, laboratory analysis in Managua; LVR, PCR testing in Ghent, contributions to the manuscript; MT, overall supervision, interpretation of results, final reading of the manuscript

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Accepted for publication 13 December 2001

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