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Pap smear prevalence and that of pre-malignant and malignant cervical lesions amongst women living in the Carmen initiative demonstration area, Bucaramanga, Colombia


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SUMMARY

Objective: Establishing the prevalence of pre-malignant and malignant cervical lesions amongst women living in the CARMEN initiative demonstration area, Bucaramanga, Colombia.

Methodology: A cross-sectional study of 8,015 randomly selected women. Patients having abnormal cytology results received individualised diagnosis/treatment (colposcopy, biopsy, or conisation). Histopathological findings were correlated with demographical data and their sexual and reproductive history.

Results: 8,071 women answered the survey but only 2,698 had up-to-date Pap smears (34.9%; 95%CI 17.2%-29.8%); 1,660 accepted updating their smears. 2.2% (95%CI 1.8%-2.6%) had Pap smears positive for cervical lesions, this being higher in those living with more mature women. Pre-malignant and malignant cervical lesion prevalence was 1.1% (95%CI 0.8%-1.4%). Women with pre-malignant or malignant cervical lesions were younger, had begun their sexual intercourse earlier and had had more sexual partners than healthy women.

Conclusions: Pre-malignant and malignant cervical lesion prevalence is higher than in other parts of the world. Pap smear coverage is very low. Early detection of cervical cancer must be intensified.

Keywords: cervical neoplasia, CIN, cervico-vaginal cytology, human papillomavirus.

RESUMEN

Objetivo: Establecer la prevalencia de lesiones premalignas y malignas entre las mujeres que viven en el área demostrativa de la iniciativa CARMEN de Bucaramanga, Colombia.
Metodología: Estudio trasversal de 8.015 mujeres seleccionadas al azar. Las pacientes con citología anormal fueron estudiadas y tratadas de manera individualizada según un protocolo que incluía colposcopia, biopsia o conización. Se hizo correlación histopatológica con las variables sociodemográficas y la historia sexual y reproductiva.

Resultados: 8.071 mujeres contestaron la encuesta, pero solo 2.698 tenían una citología reciente (34,9%; IC 95% 17,2%-29,8%); 1.660 actualizaron su citología. 2,2% de estas fueron positivas, siendo más alta entre las mujeres que viven con otras mujeres adultas. La prevalencia de lesiones pre-malignas y malignas del cuello uterino fue 1,1% (IC 95% 0,8%-1,4%). Las mujeres con lesiones cervicales pre-malignas o malignas eran más jóvenes, habían iniciado relaciones sexuales más temprano y habían tenido más compañeros sexuales que las mujeres sanas.

Conclusiones: La prevalencia de lesiones cervicales pre-malignas y malignas es superior a la que se informa en otras partes del mundo, mientras que la cobertura de citología cérvicovaginal es muy baja. Es necesario intensificar las actividades que buscan la detección temprana de cáncer cervical.

Palabras clave: Neoplasia cervical, NIC, citología cérvicovaginal, papilomavirus humano.

INTRODUCTION

Cancer is the second cause of death among Colombian women and cervical cancer is the second cause following breast cancer.1 The crude annual cervical malignant tumour rate in Bucaramanga (Colombia) was 22.3/100,000 inhabitants (adjusted rate 25.1/100,000 inhabitants) in 2000–2001, the second most frequent cancer in the region after breast cancer.2

Cervical cancer and pre-malignant lesions behave as a sexually transmitted disease, associated with human papillomavirus infection, although certain genetic susceptibility has also been reported.3 Cervical cancer programmes lead to decreased incidence and mortality rates because of early detection, including overcoming obstacles at personal, social and health system level blocking access to screening and diagnosis.4,5

At present, there are few population-based studies on malignant or pre-malignant cervical lesion prevalence or related to the prevalence of abnormal cytology. Duello et al., in 1979, found 2.04% pre-malignant lesion prevalence in 411 women autopsied in Cali, Colombia.6 Molano et al., in their 2002 study of the natural history of human papillomavirus infection in Bogotá, reported 150 out of 2,110 women having abnormal cytology, a 7.11% prevalence.7 This is why the Secretary of Health and Environment for Bucaramanga (a city having 600,000 inhabitants, located in north-eastern Colombia) decided to carry out a cross-sectional survey to establish malignant or pre-malignant cervical lesion prevalence and associated factors and that for Pap smear use in women living in the city.

METHODOLOGY

A survey was carried out among women aged 15 to 65 living in the CARMEN Initiative’s demonstration area in Bucaramanga. The CARMEN (Conjunto de Acciones para la Reducción Multifactorial de las Enfermedades no Trasmisibles) Initiative is a programme aimed at improving the city’s health by reducing risk factors associated with non-transferable illnesses by means of population intervention. It is similar to WHO’s Cindy Programmes in other countries. The demonstration area was designed to establish a baseline and test such interventions designed according to initial findings, including health resources and community networks.

This research was approved by the Universidad Autónoma de Bucaramanga’s Medicine Faculty Review Board; each participating woman signed an informed-consent form.

Expected malignant or pre-malignant cervical lesion prevalence was 1.0%±0.1% and alpha probability for sample calculation was 0.05. All the 8,666 houses in the CARMEN area were visited. In houses having more than one woman, only one was selected.
by applying a random number list. A self-applicable survey was designed for collecting demographical data, including social security system affiliation, knowledge of vaginal cytological examination and sexual and reproductive history.

It was considered that the cervical Pap smear test was indicated for those women who were older than 17, or younger if they had already had sexual intercourse. Women were encouraged to undertake free-of-charge cytological examination if they had not had one taken during the last year. If she had undergone the examination but it was noticed that the results had questionable quality or were not available, cytological examination was also recommended. No further or new examinations were required when cytological examination had been undertaken within the year prior to the survey and good quality results were available. Such result was accepted for this survey.

All slides were read by an expert cytological technician as part of her regular work. All positive or suspicious results, according to Bethesda’s classification system, were blind checked by a pathologist, as well as a 10% sub-sample taken at random from negative result samples for quality control. If cytological results were normal, patients were instructed to continue submitting themselves to this exam, according to the most convenient time interval. If negative results were obtained for malignity but positive for any benign lesion, the patient was treated according to each particular case. In all the women with abnormal cytology for pre-malignant or malignant cervical lesions, a colposcopy/biopsy was carried out to confirm the diagnosis. Patients whose histopathological results confirmed a high-grade squamous intraepithelial lesion were referred to their health insurance companies for follow-up and treatment.

The information collected was put into a database and a duplicate made. Frequency charts were defined and continuous variables’ averages and standard deviations (SD) were calculated. Cervical lesion prevalence rates were calculated with their 95% confidence interval (95%CI) and prevalence rates (PR) for sexual and reproductive characteristics. A binomial regression was made to control potential confounding for the presence of pre-malignant/malignant lesions. A statistical significance test was used when making comparisons, if necessary (Student’s t, χ² or linear χ²), having a < 0.05 acceptance level. Stata 9.0 was used for statistical analysis of the data.

RESULTS

8,071 women answered the survey. Only 2,698 women had updated Pap smear results (34.9%; 95%CI 17.2%-29.8%); 1,660 accepted updating their cytology. 4,358 women had had recent cervical cytological examination (54.8% coverage, 95%CI 53.4%-56.4%). Their average age was 37.0 (SD 13.4). 13.3% had undergone higher education whilst only 33.1% had had access to some elementary education. 59.8% stated that they were married and 21.8% were single. 49.0% said they were the head of their families. 12.5% of their partners had had some levels of university education whilst 42.3 % had not had access to secondary education.

7,330 out of 7,978 adult women (91.9%, 95%CI 91.3%-92.5%) admitted to having had sexual intercourse; 126 (30.9%) out of 408 girls aged less than 18 had had sexual relations. The average age for the first sexual intercourse was 19.0 (SD 3.8); 81.9% (95%CI 81.0%-82.74%) had been pregnant at least once.

83.9% (95%CI 83.1%-84.7%) of the women had undertaken a cervical Pap smear at least once in their lives; 77.6% women had spontaneously requested their last examination (95%CI 76.5%-78.6%). 442 women (6.6%, 95%CI 6.0%-7.3%) had had abnormal results from at least one Pap examination. 34 out of the 8,015 women reported having experienced the “beginning” of cervical cancer at least once in their lives. 66.1% of the women (95%CI 65.1%-67.2%) had a regular pattern regarding the Pap smear, whilst the remaining 33.9% had undergone the process occasionally or had never submitted to it.
4,346 out the 7,733 women had recent and valid Pap smear results. 94 (2.2%, 95%CI 1.8%-2.6%) were positive for possible pre-malignant/malignant lesions (Table 1). 161 (10.2%) out of the 1,573 normal cytological results were re-examined as part of the quality control strategy. Normality was confirmed in 157 slides (97.5%, 95%CI 93.8%-99.3%). Two of the rejected slides corresponded to ASCUS and another two were rejected due to inappropriate sampling.

Abnormal Pap smear cytology prevalence in women who lived without other adult women was 0.8% (95%CI 0.4%-1.3%), but prevalence was higher in those who lived with other adult women: 0.9% for one woman (95%CI 0.4%-1.5%), 1.4% for two (95%CI 0.7%-2.5%), 1.9% for three (95%CI 0.6%-4.3%) and 3.4% for four or more women (95%CI 0.9%-8.0%; p=0.067). No differences were found in abnormal Pap smear prevalence for other demographic characteristics, knowledge and experience concerning Pap smear cytological examination and sexual or reproductive history.

Six out of the 94 women having suspiciously malignant results in their cervical examination did not attend the colposcopic control session despite all the team’s efforts to get them to attend (missing ratio: 6.4%, 95%CI 5.4%-13.4%); these six women had a CIN 1 Pap smear. 46 out of the 88 women with suspiciously malignant results who attended the medical control session were diagnosed as being malignant by histopathology (52.3%, 95%CI 41.4%-63.0%). Overall pre-malignant/malignant lesion prevalence was 1.1% (95%CI 0.8%-1.4%); 24 women had CIN 1 (5.2%), three CIN 2 (6.5%), six CIN 3 (13.0%), twelve in situ cancer (26.1%) and one had invasive cancer (2.2%).

Figure 1. shows pre-malignant or malignant cervical lesion prevalence by age group. Women with pre-malignant or malignant cervical lesions were younger than healthy women (33.4 [SD 10.2] cf 39.7 [SD 12.7] years old (p < 0.001), had initiated sexual intercourse much earlier and had had more sexual partners than women who did not have these lesions (Table 2). Greater malignant and pre-malignant cervical lesion prevalence was found amongst women having no access to social security services compared to those women affiliated to a social security system: 1.47% cf 0.79% (PR 1.86, 95%CI 1.04–3.32, p=0.034). The multivariate model indicated that only two factors were associated with malignant or pre-malignant cervical

<table>
<thead>
<tr>
<th>Finding</th>
<th>Cases</th>
<th>Prevalence</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suspicion of malignity</td>
<td>94</td>
<td>2.2%</td>
<td>1.8% - 2.6%</td>
</tr>
<tr>
<td>ASCUS</td>
<td>40</td>
<td>(42.6%)</td>
<td></td>
</tr>
<tr>
<td>AGUS</td>
<td>1</td>
<td>(1.1%)*</td>
<td></td>
</tr>
<tr>
<td>CIN I</td>
<td>45</td>
<td>(47.9%)*</td>
<td></td>
</tr>
<tr>
<td>CIN II</td>
<td>5</td>
<td>(5.3%)*</td>
<td></td>
</tr>
<tr>
<td>CIN III</td>
<td>2</td>
<td>(2.1%)*</td>
<td></td>
</tr>
<tr>
<td>In situ carcinoma</td>
<td>1</td>
<td>(1.1%)*</td>
<td></td>
</tr>
<tr>
<td>Fungi</td>
<td>396</td>
<td>9.1%</td>
<td>8.3% - 10.0%</td>
</tr>
<tr>
<td>Gardnerella</td>
<td>153</td>
<td>3.5%</td>
<td>3.0% - 4.1%</td>
</tr>
<tr>
<td>Trichomonas</td>
<td>4</td>
<td>0.09%</td>
<td>0.03% - 0.24%</td>
</tr>
<tr>
<td>Actynommices</td>
<td>2</td>
<td>0.05%</td>
<td>0.01% - 0.13%</td>
</tr>
<tr>
<td>Papillomavirus</td>
<td>33</td>
<td>0.8%</td>
<td>0.5% - 1.1%</td>
</tr>
</tbody>
</table>

*Percentage calculated on the 94 cytology examinations from Pap smears classified as suspicion of malignity.
Table 2. Some sexual and reproductive characteristics according to presence of pre-malignant/malignant lesions

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Pre-malignant/malignant lesions</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td>P</td>
</tr>
<tr>
<td>Number of pregnancies*</td>
<td>2.7 ± 2.1</td>
<td>2.9 ± 2.3</td>
<td>0.696</td>
</tr>
<tr>
<td>Number of miscarriages*</td>
<td>0.2 ± 0.6</td>
<td>0.3 ± 0.6</td>
<td>0.781</td>
</tr>
<tr>
<td>Number of vaginal births*</td>
<td>2.2 ± 2.1</td>
<td>2.8 ± 2.2</td>
<td>0.718</td>
</tr>
<tr>
<td>Number of Caesarean sections*</td>
<td>0.3 ± 0.7</td>
<td>0.3 ± 0.5</td>
<td>0.548</td>
</tr>
<tr>
<td>Number of sexual partners**</td>
<td>1.6 ± 0.8</td>
<td>1.4 ± 1.5</td>
<td>0.017</td>
</tr>
<tr>
<td>Age first experience of sexual intercourse**</td>
<td>17.8 ± 2.7</td>
<td>19.2 ± 3.8</td>
<td>0.020</td>
</tr>
<tr>
<td>Age of first Pap smear examination***</td>
<td>23.0 ± 5.9</td>
<td>24.4 ± 7.0</td>
<td>0.228</td>
</tr>
<tr>
<td>Having sexual intercourse</td>
<td>45/4,251 (1.1%)</td>
<td>0/82 (-)</td>
<td>0.349</td>
</tr>
<tr>
<td>Having been pregnant</td>
<td>4/452 (0.9%)</td>
<td>41/3,875 (1.1%)</td>
<td>0.487</td>
</tr>
<tr>
<td>Having had more than one sexual partner</td>
<td>16/943 (1.7%)</td>
<td>23/2,748 (0.8%)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

* Calculated amongst women who have been pregnant.
** Calculated amongst women who have had sexual intercourse.
*** Calculated amongst women who have submitted to at least one cytological examination.

Figure 1. Malignant and pre-malignant lesion prevalence by age.
lesion; there was less probability for each year of delay in initiating sexual intercourse beginning at age 15 (PR 0.899; 95%CI 0.809–0.999, p=0.047) and having had three or more sexual partners (PR 2.632, 95%CI 1.072–6.462, p=0.035).

DISCUSSION
The Early Detection Cervical Cancer Programme in Colombia covers women aged 25 to 69, including sexually active younger women. The low updated Pap smear coverage found was interesting (34.9%), only increasing to 56.45% after intense motivation. This coverage is much lower than Pap smear prevalence reported in some countries. Coverage in the USA has been about 80% during the last two years and 90% at some point in most women’s lives; Pap smear coverage in Iceland is almost 100% whilst national prevalence at least once in their lives ranges from 46.7% to 53% in Mexico.

Patients who had alterations in their Pap smear tests and decided not to continue with follow-up accounted for 6.4% of the women. This results fall below the figure reported by some authors in similar studies where it ranged from 30% to 44%. Cytological lesion prevalence in our region was 2.2%, which is lower than results reported from Bogota, but similar to other Latin-American figures. The differences between our figures and Molano’s figures could be related to the slide-reader’s academic level: expert cytopathologist in Bogotá and cytology technician in Bucaramanga. However, quality control suggested no false negative screening regarding high grade lesions.

HPV cytology prevalence was much lower than expected. This situation might be explained by technical and training difficulties related to diagnosis. ASCUS prevalence (0.9%) was lower than the prevalence reported by pathology laboratories in the USA where it has been found to be closer to 2.1% or to even reach 9.0% in the high-risk population.

Global NIC I cytological prevalence was 1.0%, NIC II was 0.1%, and NIC III was 0.04%. In situ carcinoma prevalence was 0.02% and AGUS was 0.02%. These data can be compared with information reported in the USA for abnormalities in Pap smears in which 1.6% corresponded to low grade squamous intra-epithelial lesions and 0.45% to high-grade squamous intraepithelial lesions.

Molano et al., have reported results for smears taken at recruitment in their human papillomavirus study in Bogota as being 92.5% normal, 3.5% LSIL, 1.5% ASCUS, 0.7% AGUS, 0.4% HSIL, 0.1% invasive cervical cancer and 1.3% inadequate Pap smear.

Our quality control indicated very high concordance (97.5%). Correlation percentages reported in some publications range from 87% to 97%. However, Pap smear examination and biopsy carried out by colposcopy revealed correlation with Pap smear in only half of the examined specimens. Such results could be related to alterations during sample taking or to concomitant lesions such as inflammation or the place where the biopsy was taken that brought about changes in the cells.

If it is assumed that the six patients who did not attend the control sessions did not have any malignant or pre-malignant lesion (the best scenario), the prevalence of both malignant and pre-malignant lesions in the target population would have been 1.1% (95%CI 0.8%-1.4%). On the contrary, if it were assumed that these six patients were sick (the worst scenario), then prevalence would have been 1.2% (95%CI 0.9%-1.6%). According to our quality control, 2 out of every 161 negative slides correspond to ASCUS and therefore 53 additional cases of Pap smear with suspicion of malignity would be found, 11 cases for every 26 Pap smears would be positive for malignant and pre-malignant lesions, this leads to 22 additional cases, plus 6 additional cases of malignity added from six women who did not attend the control sessions, leading to 72 patients with malignant and pre-malignant lesions in their cervix. Prevalence would then be 1.7% (95%CI 1.3-2.1%).

Based on this analysis, preneoplastic and neoplastic lesion prevalence amongst the studied
population would be between 0.8% and 2.1%. This situation cannot easily be compared to world statistics. Although there are many reports available about cases diagnosed as having cancer, there are few reports regarding prevalence in populations. The SEER Cancer Statistics Review reports gross cervical cancer prevalence in the USA of 11.68 per 10,000 women. This figure is very similar to the data reported for Asia where preneoplasic and neoplasic cervix lesion prevalence is 11 per 10,000 women. Prevalence was at least 66 cases per 10,000 women in our case. This means that the study population from Bucaramanga greatly surpassed the figures for the USA and Asia.21

It is worth stressing that lacking suitable knowledge of the Pap smear, as well as refusal to actively participate in early detection programmes, did not discriminate women having cervical lesions from women who did not share these views. Such situation did not correspond to the findings of a population study in Mexico where it was concluded that participation in these educational programmes would reduce the probability for women to develop malignant cervix neoplasia by 2.8 times, proportional to the number of regular check-ups.19

The age at which sexual activity is initiated (19 years old on average) was very similar to the age reported from other parts of the world. This is a very important risk factor for the development of cervix preneoplasic and neoplasic lesions, as reported by Hulka who found that initiating sexual activity before age 20 is the most important and consistent risk factor.20 As reported from other areas of the world, patients with pre-malignant and malignant cervix lesions have a larger number of sexual partners, initiate their sexual activity at an earlier age and present higher alcohol intake.21-23

Our findings contrast with the information published in Mexico, where a direct relationship was found between submitting to Pap tests and the literacy level of women and their sexual partners.24 Such phenomenon has also been observed in Cuba where an important factor for women’s participation is to know how helpful the test is, which is directly connected to their literacy level.25

The institutions responsible for supplying health services are frequently referred to as being the providers of Pap smear knowledge.20 However, based on the level of effective knowledge and commitment to programmes, either as a previous or as a direct response to a stimulus such as the issue dealt with in this research, it can be stated that there must be a greater spread of information at all levels, especially through companies responsible for providing health services and through educational institutions which, at present, are not acknowledged as being important parties in spreading information about Pap smear exams and cervical cancer.26 Considering the social category of the populations studied in this research, it is possible to conclude that the educational components related to sexually transmitted diseases and family planning programmes are differently assumed by people. This differential impact goes against Pap smear examination. It is important to remember that becoming older is the most important barrier preventing women from participating in diagnostic testing.27

What should be done to improve the situation found in this research? Few very important activities yielding a great impact can be proposed:28,29 increasing programme coverage using motivation and active user search; establishing an ongoing information and educational network; educating the community in aspects related to cervical cancer risk factors and establishing an ongoing surveillance program regarding this pathology; getting women’s partners actively involved in these strategies; establishing a support strategy at Secretary of Education or Health level; and increasing the scope of being able to enrol in a social and health security system.

REFERENCES


**Conflict of interest:** This research work was sponsored by the Secretary of Health and the Environment, Bucaramanga, Colombia.