

Prevalence of high-grade cervical intraepithelial neoplasia in Mexican women aged under 40 years: a cross-sectional study

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Abstract

Objective: Cervical cancer is the second leading cause of cancer mortality among Mexican women aged 20-39 years, driven primarily by persistent human papillomavirus (HPV) infection. To determine the prevalence of high-grade squamous intraepithelial lesions (HSIL) in women under 40 years of age and identify associated risk factors.

Material and Methods: An observational, cross-sectional study was conducted, including 359 women under 40 years old who were evaluated at the Gynecology and Obstetrics Medical Unit of Centro Médico Nacional de Occidente. Cervicovaginal cytology results indicative of HSIL were analyzed to determine prevalence and assess correlations with demographic and gynecological factors.

Results: The prevalence of HSIL was 39%, with the highest proportion of cases observed in women aged 35-39 years. The average age of sexual debut was 18.5 years, with an average of 2.93 sexual partners. Women diagnosed with HSIL were more likely to be older, married, and homemakers. HPV infection was highly prevalent across both low-grade squamous intraepithelial lesion and HSIL groups.

Conclusion: A high prevalence of HPV infection was found, mostly in a relatively young population. A significant association between infection and risk factors, like marital status and gynecological/obstetric history, was also demonstrated. The findings also confirmed a relationship between HPV and HSIL. [J Turk Ger Gynecol Assoc. 2025; 26(3): 167-73]

Keywords: Pap smear, cervical cancer, cervical intraepithelial lesion, HSIL, cervical screening

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Introduction

Among women aged 20-39 years, cervical cancer (CC) is the second leading cause of cancer mortality, causing 10 deaths per week (1). In Mexico, CC was the second leading cause of death in women, with an estimated 9,439 new cases and 4,335 deaths in 2020 (2). Most cases in the country are diagnosed at the locoregional stage (3).

Persistent infection by carcinogenic types of human papillomavirus (HPV) is the main cause triggering CC development (4). HPV in the cervical epithelium causes alterations in the host genome, leads to downregulated tumor suppressor factors, and induces aberrant functioning of several tumor-promoting factors (5).

The transformation zone at the junction between the ectocervix and endocervix (i.e., the squamocolumnar junction) serves as the usual origin of cervical lesions (6). Cervical preneoplasia, also called cervical intraepithelial neoplasia (CIN), corresponds to low-grade squamous intraepithelial lesions (LSIL) or high-grade squamous intraepithelial lesions (HSIL). In the latter, the extent and degree of atypia generally exceed the limits described in flat or exophytic condylomas (7,8).

Early detection is essential to identify the disease in its early stages when it is more treatable and associated with better outcomes. This can be achieved by cytology or HPV testing to identify cervical cell abnormalities. The pap smear test reveals cervical cell morphological alterations that indicate precancerous changes, while the HPV test detects the presence of the virus based on its genetic material in cervical cells, with a sensitivity of 90% for precancer detection. In both cases, follow-up colposcopy is necessary to identify precancerous lesions (9,10).

According to the American Cancer Society, the recommended age to initiate screening is 25 years, and a primary HPV screening test is recommended, as is a concomitant test or cytology alone (11). However, considered as screening after the age of sexual activity onset, which detects more than 97% of young women (12).

In unscreened women, the prevalence of LSIL tends to decrease with age. In contrast, the rates of HSIL tend to increase with age, establishing the importance of performing such cancer screening tests early (13).

In Latin American countries, screening coverage in 2019 was over 50%, as early testing, including annual cytology, is performed according to national recommendations (14). In Mexico, it is estimated that about 4.1% of women in the general population harbor a cervical HPV- 16/18 infection at any given time, while 65% of invasive CCs are attributed to HPV- 16/18. In addition, there is a population of 49.6 million women aged 15 years and older who are at risk of developing CC (15). Therefore, timely detection of cervical lesions in the young

female Mexican population is of great public health importance. The aim of this study was to determine the prevalence of HSIL in a cohort of patients aged under 40 years.

Material and Methods

For this cross-sectional, observational study, patients were included from January 1, 2019, to January 1, 2023. The study focused on women aged under 40 years who were evaluated at the Gynecology and Obstetrics High Specialty Medical Unit of the National Western Specialty Hospital, Mexican Social Security Institute. These patients underwent cervicovaginal cytology, either for screening purposes or as part of the protocol for gynecologic hysterectomy, and their results corresponded to an HSIL. In accordance with the journal's guidelines, we will provide our data for independent analysis by a selected team by the editorial team for the purposes of additional data analysis or for the reproducibility of this study in other centers, if such is requested.

Patient selection

Female patients under 40 years of age were included if they had undergone cervicovaginal cytology. Exclusion criteria included patients aged 40 years and older, those with immunosuppressive conditions (e.g., HIV infection or autoimmune diseases), or patients receiving immunosuppressive or immunomodulatory therapies, which may alter susceptibility to or increase the risk of cervical premalignant or malignant lesions.

Measuring instruments

Cervical cytology samples were collected using two techniques. The first technique employed the Ayre spatula for exocervical sampling. The bifurcated end of the spatula was inserted into the cervical orifice and rotated 360° clockwise with gentle pressure to ensure a comprehensive sample of the exocervical epithelium, paying particular attention to irregular areas. For endocervical sampling, the conical portion of the spatula was inserted into the cervical canal and rotated 360° counterclockwise. The sample was then spread onto a slide and fixed with 96% alcohol.

The second technique used an endocervical brush or swab, which was gently introduced into the cervical canal, rotated clockwise, and then removed for sample placement onto a slide. To ensure sample adequacy, specimens had to contain cells from the transformation zone. Samples were deemed inconclusive if the transformation zone was everted or significantly reduced. In cases where the transformation zone was retracted into the endocervical canal, a cotton swab moistened with physiological saline or sterile water was used. The cytological results were classified using the Bethesda system and correlated with the Mexican official standard (NOM-014-SSA2-1994). All cytology slides were reviewed

by a cytopathologist, and results were categorized as either low-grade intraepithelial lesions (e.g., HPV, mild dysplasia, CIN 1) or high-grade intraepithelial lesions (e.g., moderate dysplasia, severe dysplasia, carcinoma *in situ*, CIN 2, CIN 3). HPV infection was confirmed by the identification of hallmark cytopathological changes, including koilocytosis, dyskaryosis, and nuclear enlargement.

Statistical analysis

The results are expressed as mean and standard deviations (SDs) or numbers and percentages. Descriptive statistics were calculated using percentages for categorical variables and means $\pm$ SDs for continuous variables. Categorical data were analyzed using the chi-square test. Differences were considered significant at $p < 0.05$. All odds ratios (ORs) were given with 95% confidence intervals (CIs). SPSS, version 21 (IBM Corp., Armonk, NY, USA) was used for statistical analyses.

Ethical considerations

The study adhered to the stipulations of the 2013 Declaration of Helsinki and its amendments, the General Health Law, and the regulations of the host institution regarding research in humans. The study was approved by the Research and Ethics Committee of the Instituto Mexicano del Seguro Social (approval number: R-2022-1301-123, date: 23.01.2022).

Results

A total of 359 patients aged under 40 years who met all inclusion criteria were included. The mean age was 32.5 ± 5.37 years. The youngest patient was 15 years old, and the biggest age group was 35-39 years making up 42.3% of the sample, while the group with the lowest representation was aged 15-19 years (Figure 1).

In terms of marital status, 162 (45.1%) reported that they were married, followed by 124 single patients (34.5%). Two hundred fifty-seven (71.6%) reported having a paid job, 98 (27.3%) were homemakers, and 4 (1.1%) were students (Table 1).

Regarding comorbidities, 296 (82.5%) reported having none, 11 (3.1%) reported having hypertension, 8 (2.2%) reported having hypothyroidism, and 7 (1.9%) reported having type 2 diabetes mellitus. Additionally, 28 (7.8%) reported having two or more chronic diseases. The mean patient body mass index was 26.7 ± 5.02 kg/m². Forty-six (12.8%) reported active smoking.

The obstetric and gynecological history of the sample is listed in Table 2. Twenty-nine percent reported never having been pregnant, followed by 21.7% with two pregnancies. The least common parities were 7 and 8, with one patient in each case. The mean age of sexual activity onset was 18.5 ± 3 years, with a mean of 2.93 ± 1.85 sexual partners. The most frequent number of sexual partners was 2 or 3.

Table 1. Sociodemographic characteristics

Marital status	Number of patients	%
Married	162	45.1
Divorced	14	3.9
Single	124	34.5
Cohabiting	56	15.6
Widow	3	0.8
Occupation		
Paid employment	261	72.7
Homemaker	98	27.3

Table 2. Obstetrical and gynecological history

	Number of patients	%
Gestations		
0	104	29
1	72	20.1
2	78	21.7
3	56	15.6
4	35	9.7
5	9	2.5
6	3	0.8
7	1	0.3
8	1	0.3
Family planning method		
None	155	43.2
Abstinence	1	0.3
Contraceptive ring	2	0.6
IUD	22	6.1
Medical IUD	7	1.9
Injected hormone	3	0.8
Oral hormonal	17	4.7
Subdermal implant	21	5.8
BTO	60	16.7
Patches	16	4.5
Preservative	55	15.3
Number of sexual partners		
1	81	22.6
2	90	25.1
3	90	25.1
4	43	12
5	27	7.5
6	12	3.3
7	3	0.8
8	5	1.4
9	0	0
10	8	2.2

IUD: Intrauterine device, BTO: Bilateral tubal occlusion

Regarding family planning, 43.2% of the sample reported not using any contraceptive method, 16.7% had bilateral tubal occlusion, 15.3% used condoms, and 5.8% used a subdermal implant as their family planning method.

The most prevalent gynecological diseases were endometriosis and uterine myomatosis (2.5% and 2.2%, respectively), while 81.9% reported no history of gynecological disease. HPV infection was present in 87.7% of patients and thus only 4.2% were not carriers of the infection.

All patients had a diagnosis by exfoliative cytology (Figure 2). Regarding the prevalence of cytological diagnoses by age group, older patients (30-39 years) more commonly presented with HSIL ($p=0.016$; OR, 1.723; 95% CI: 1.067-2.783) compared with younger patients (15-29 years). There was a higher percentage of patients who were homemakers in the group

who did not have HSIL ($p=0.001$; OR, 2.356; 95% CI: 1.467-3.782). Other variables are shown in Table 3.

There were no significant between-group differences in histo/cytopathological history, although the percentage of patients with some chronic disease was higher in the group with HSIL (22.9% versus 14.16% in the group without HSIL). The HSIL group $n=140$ (39%) also included a higher percentage of tobacco users $n=128$ (91.4%) including those who had former use or were active smokers at the time of the study compared with $n=185$ (84.5%) in the group without HSIL.

Finally, the group with HSIL was more likely to use family planning methods, with the intrauterine device most common (10%, contrasted with 3.7% in the group without HSIL). The HPV infection distribution was similar between these groups.

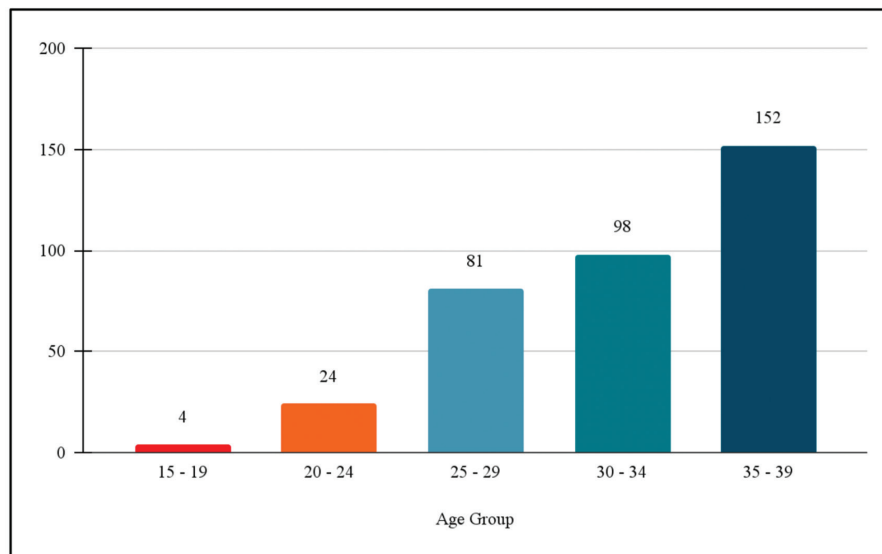


Figure 1. Participant distribution by age group

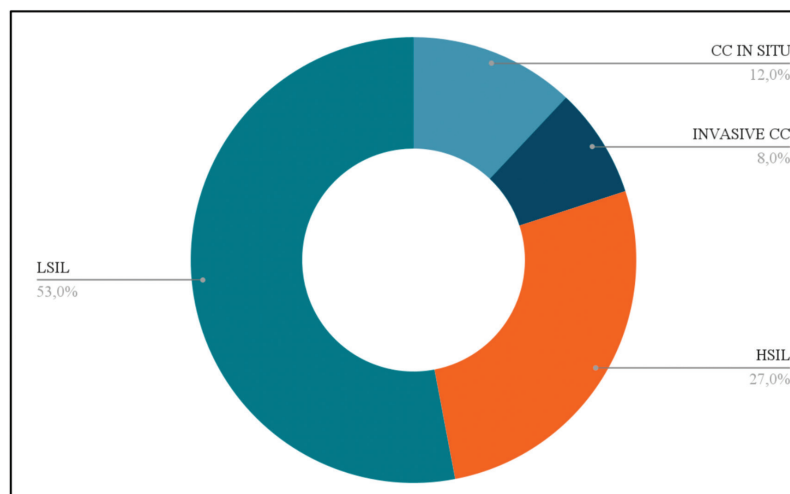


Figure 2. Distribution of diagnoses by cytology

LSIL: Low-grade squamous intraepithelial lesions, HSIL: High-grade squamous intraepithelial lesions, CC: Cervical cancer

Table 3. Analysis of variables

	HSIL	No HSIL	Total	p-value	OR	95% CI
Age of onset of sexual activity						
≤17 years	52	70	122	0.185*	0.795	0.509-1.241
18–39 years	88	149	359			
Number of sexual partners						
≤3 partners	103	158	261	0.432*	0.930	0.577-1.501
≥4 partners	37	61	98			
Number of pregnancies						
≤2 pregnancies	95	159	254	0.199*	1.255	0.790-1.994
>3 pregnancies	45	60	105			
*p-value calculated with chi-square test. HSIL: High-grade squamous intraepithelial lesion, OR: Odds ratio, CI: Confidence interval						

Discussion

HSIL has been shown to be remarkably predictive of CC development. As such, early identification of lesions, particularly in early life, is critical for preventing the establishment of malignant disease.

Herein, the average age of the study sample was 32.5 years, with the youngest patient being 15 years old at diagnosis. In the study by Bonas et al. (16) of patients younger than 30 years, 46 were younger than 25 years and 20 were aged 25-30 years. Thus, the youngest patients were most prevalent in their study, in contrast with the present study in which the most highly represented age group was women aged 35-39 years (152 patients) and there were only four patients in the 15-19 years age group. This finding aligns with that of, Possati-Resende et al. (17) who reported a mean age of 37.9 years for patients with HSIL.

Kalavathy et al. (18) divided patients according to marital status (i.e., living with or without a husband). The group not living with a husband predominated, with 53.8%. Herein, the marital status of patients with HSIL was in contrast to that reported by Kalavathy et al. (18) that is, married patients made up 45.1% of our total sample. According to our findings and those of Darré et al. (19), married women and those whose occupation is homemaker may engage in more regular sexual activity, increasing their risk of developing precancerous cervical lesions. Similarly, Ssedyabane et al. (20) reported a higher prevalence of cervical lesions among married women compared with those with a different marital status.

The mean number of gestations in our study was 1.7 ± 1.5 . Twenty-nine percent were nulligravid and 78 (21.7%) had two pregnancies. Patients with seven or eight gestations were less common, with one patient in each case. Mukhtar et al. (21) highlighted that one-third of the women in their sample were nulligravid (31.9%). The median gestational age of their pregnancies was 30.5 weeks.

In their sample, 97.8% had only one sexual partner. Five hundred and two patients (85.5%) initiated sexual intercourse between the ages of 20 and 30 years. Compared with our cohort, the age of sexual activity was 18.5 (± 3) years and the average number of sexual partners was 2.93 (± 1.85). These results might be explained by cultural differences. The relevance of gynecological/obstetric characteristics and history is in the important associations between them and possible cytological changes. As described by Rasheed et al. (22), a significant association was found between cervical cytology results and advanced age, increased number of sexual partners since coitarche, and parity.

Alarcón-Romero et al. (23) reported an overall HPV prevalence of 54.16%, while 91.39% of patients with HSIL were HPV-positive. This is similar to our findings, in which 87.7% of the sample was HPV-positive. Similarly, Campos et al. (24) reported that 79.2% of their patients had HPV infection, including those with normal cytology, LSIL, HSIL, and CC.

According to Xu and Wang (25), there was a higher prevalence of HPV infection (98.0%) in their group with CIN (26). HPV infection was also significantly more prevalent in older age groups compared with perimenopausal patients, mainly due to factors such as sexual behavior, educational level, history of genital tract diseases, multiple pregnancies, contraceptive methods without tubal ligation, and postcoital hygiene practices.

Herein, diagnoses according to exfoliative cytology were LSIL in 53% and HSIL in 27%, followed by 12% with cancer *in situ*, and 8% with invasive cancer. In the study by Mishra et al. (27), the histological abnormalities were LSIL in 950 (11.52%) patients, HSIL in 851 (10.32%) patients, and CC in 207 (2.51%) patients. Consistent with our results, that group reported that the most frequent cytological diagnosis was LSIL, followed by HSIL, and then some cancer types. However, we differentiated cancer *in situ* and invasive cancer into different groups.

We recognize the limitations of our study regarding the HPV diagnostic method. Although exfoliative cytology varies based on coinfection, diagnosis by other methods like polymerase chain reaction would allow viral identification even before cervical modifications appear and distinguish virus strains. This study showed the presence of HSIL diagnosis and the presence of HPV infection, in addition to sociodemographic characteristics that are consistent with the international literature. We also recognized our limitations on the sample and the number of patients included, due to some deficiencies of the care unit itself, thus we encourage to further explore this topic on a larger scale. The cumulative findings support the importance of determining these characteristics in the Mexican population, toward prevention and timely detection.

Implications for practice and policy

The findings of this study underscore the crucial role of early detection and prevention strategies in reducing the incidence of CC among young women. Routine screening through HPV testing and cytological analysis is essential for the timely identification of HSIL, which is highly predictive of CC development. For healthcare practitioners, integrating HPV testing with cytology as part of routine cervical screening, particularly in women aged 25 and older, should be prioritized to ensure early detection and intervention, which can significantly improve patient outcomes and reduce the risk of CC progression. In addition, practitioners should leverage the study's findings that link sociodemographic factors, such as marital status and parity, to increased HSIL risk. This information can be used to target high-risk groups with more tailored educational and screening interventions.

This study highlights the need to strengthen national screening programs and expand access to routine cervical screening services, especially in areas with below-optimal coverage. Moreover, vaccination policies should focus on increasing accessibility to the HPV vaccine, particularly for adolescents, to prevent infections linked to CC. Public health campaigns should raise awareness about the importance of HPV vaccination and regular CC screening to promote early detection and adherence to screening guidelines.

Future research and implementation strategies must prioritize culturally sensitive and accessible screening programs for underserved populations. Policymakers must wholeheartedly support ongoing research into the effectiveness and cost-efficiency of HPV screening and vaccination programs to seamlessly integrate them into healthcare systems.

These efforts will be central to significantly reduce the incidence of CC and thus improve health outcomes for at-risk women.

Study limitations

The limitations of our study were the retrospective design and the lack of evaluation of molecular markers to confirm the results.

Conclusion

Our sample of relatively young adults, with an average age of 32.5 years, had a high prevalence of HPV infection (87.7%). A significant association was observed between HSIL and risk factors including age, marital status, and gynecological/obstetric history. Furthermore, the relationship between HPV infection and diagnosis of HSIL was confirmed. Although the results regarding the distribution of lesions and cytological diagnoses are consistent with the international literature, they highlight the need for more sensitive HPV diagnostic methods.

Ethics

Ethics Committee Approval: *The study was approved by the Research and Ethics Committee of the Instituto Mexicano del Seguro Social (approval number: R-2022-1301-123, date: 23.01.2022).*

Informed Consent: *The study adhered to the stipulations of the 2013 Declaration of Helsinki and its amendments, the General Health Law, and the regulations of the host institution regarding research in humans.*

Footnotes

Author Contributions: *Surgical and Medical Practices: E.G.J.P., L.P.L.T., L.G.C.B., Concept: E.G.J.P., L.P.L.T., L.G.C.B., A.G.O., C.F.O., Design: E.G.J.P., A.G.O., C.F.O., Data Collection or Processing: E.G.J.P., L.P.L.T., L.G.C.B., Analysis or Interpretation: A.G.O., E.C.P., J.M.G.D., V.T.H.R., C.F.O., Literature Search: G.C.G., E.C.P., S.R.O., S.J.V.S., S.E.G.M., K.D.M.M., J.M.G.D., V.T.H.R., A.S.A.V., C.E.C.T., Writing: E.G.J.P., S.E.G.M., K.D.M.M., J.M.G.D., V.T.H.R., A.O.C.F.*

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