

Prevalence of Chronic Diseases in Patients Diagnosed with Intraepithelial Lesion of the Cervix

Prevalencia de enfermedades crónicas en pacientes diagnosticadas con lesión intraepitelial del cérvix

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Summary

Objective: to identify the association between chronic diseases and intraepithelial lesion of the cervix in women between 25 and 60 years, in a Family Medicine Unit. **Methods:** cross-sectional analytical study, carried out from June to October 2020, through a simple random probability sampling. 533 women were included in the sample, from 25 to 60 years, with screening for cervical cancer by cervical cytology during 2019. Chronic disease was considered to be present when there was a record of personal pathological background in the clinical history or medical note in the electronic medical record. The cervical cytology result was classified as normal, based on the Bethesda System, when there was no presence of HPV or cellular atypia; low-grade lesion when there was presence of HPV and cervical intraepithelial neoplasia (CIN) 1; high-grade lesion with report of CIN 2, CIN 3 and cancer in situ. Descriptive statistics; bivariate analysis and logistic regression were performed to establish association with OR, 95% CI and p-value. **Results:** according to the cervical cytology report, it was normal in 69.8% (372/533), atypia in 3% (16/533), CIN 1 in 17.4% (93/533), CIN 2 in 5.6% (30/533), CIN 3 in 3.4% (18/533) and cancer in situ in 0.8% (4/533). The chronic conditions associated with intraepithelial lesions were BMI ≥ 30 with OR 1.3 and smoking OR 3.3. **Conclusion:** in this investigation, three out of ten women presented intraepithelial lesion in the cervix. Smoking and obesity were identified as risk factors for squamous intraepithelial lesions of the cervix.

Keywords: Cervix Uteri, Atypical Squamous Cells of the Cervix Chronic Diseases, Carcinoma In situ

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Resumen

Objetivo: identificar la asociación entre padecimientos crónicos y lesiones intraepiteliales del cuello uterino en mujeres de 25 a 60 años en una unidad de medicina familiar. **Métodos:** estudio transversal analítico, realizado de junio a octubre de 2020, mediante muestreo probabilístico aleatorio simple. La muestra se conformó de 533 mujeres de 25 a 60 años, con detección de cáncer cervicouterino por citología cervical durante 2019. Se consideró que padecían enfermedad crónica cuando existió registro de antecedentes personales patológicos en la historia clínica o nota médica de expediente clínico electrónico. El resultado de citología cervical se clasificó como normal, con base en el Sistema Bethesda, cuando no existió presencia de VPH o atipia celular; lesión de bajo grado cuando hubo presencia de VPH y neoplasia intraepitelial cervical (NIC) 1; lesión de alto grado con reporte de NIC 2, NIC 3 y cáncer in situ. Se realizó estadística descriptiva; análisis bivariado y regresión logística para establecer asociación con OR, IC 95% y valor p. **Resultados:** de acuerdo con el reporte de citología cervical, fue normal en 69.8% (372/533), atipia en 3% (16/533), NIC 1 en 17.4% (93/533), NIC 2 en 5.6% (30/533), NIC 3 en 3.4% (18/533) y cáncer in situ en 0.8% (4/533). Los padecimientos crónicos asociados a lesiones intraepiteliales fueron IMC ≥ 30 con OR 1.3 y tabaquismo OR 3.3. **Conclusión:** en la presente investigación, tres de cada diez mujeres presentaron lesión intraepitelial en cérvix. El tabaquismo y la obesidad se identificaron como factores de riesgo para lesiones intraepiteliales escamosas de cuello uterino.

Palabras clave: cuello uterino, células escamosas atípicas del cuello uterino, enfermedades crónicas, carcinoma in situ

Introduction

Chronic diseases of the cardiovascular, cancer and diabetes type constitute the leading causes of morbidity, disability and mortality; in America, in 2016, they caused 81% of all deaths, in which 39% of these people were under the age of 70.¹

Globally, cervical cancer ranks fourth in frequency in women. In 2018, there were 570,000 cases of cervical cancer and 311,000 deaths from this cause. In Central America, cervical cancer ranks third in incidence after breast and prostate cancer, being the second leading cause of cancer-related death in women; the highest cumulative risk of mortality is found in Jamaica, Bolivia, and Guyana.²⁻³ In 2018, there were 56,000 new cases in Latin America and 28,000 deaths from cervical cancer.⁴ In Mexico, the states with the highest mortality from cervical cancer are Morelos, Yucatan, Veracruz, Chiapas, and Oaxaca.⁵⁻⁶

Worldwide, squamous intraepithelial lesions of the cervix account for 10-25% of cervical cytology reports; in Mexico, the incidence is 4%.^{5,7-9} Squamous intraepithelial lesions are precursors of cervical cancer and are classified, according to the Bethesda system, into low-grade squamous intraepithelial lesions (LSIL), atypical squamous cells of uncertain significance, and high-grade squamous intraepithelial lesions (HSIL).¹⁰ LSILs spontaneously remit without management; progression from squamous intraepithelial lesion to cancer is associated with factors such as smoking, obesity, diabetes, hypertension, and Human Immunodeficiency Virus (HIV).^{11,12}

Diabetes and obesity are associated with increased risk of developing cervical cancer, the related mechanisms are: being insulin resistance, chronic hyperinsulinemia, increased bioavailability of

steroid hormones, and chronic inflammation; all of which reduce cell death and promote abnormal cell growth.¹³⁻²¹ Cigarette smoke contains carcinogenic substances, which have been found in the cervical mucosa of women who smoke with HPV infection, causing cell mutations that predispose to the development of atypia.²²⁻²⁴ Being a carrier of HIV causes a deficient immune response that does not allow HPV infection to be eliminated, which increases the risk of progression to cancer.²⁵

Family physicians play an important role in the prevention and detection of chronic diseases and premalignant cervical cancer lesions. Therefore, the objective of this research was to identify the association between chronic conditions and intraepithelial lesions of the cervix in women aged 25 to 60 years in a family medicine unit.

Methods

Cross-sectional analytical study carried out from June to October 2020, in the Family Medicine Unit (FMU) no. 26 of the Mexican Institute of Social Security in Guerrero, Mexico. The sample was calculated with a confidence level of 95%, from a total population of 4937 women registered in the Institutional Cancer Registry (RIC) platform, with cervical cancer screening in 2019, with a prevalence of 7%, obtaining a sample of 533 women. The sampling was simple random probability, the total number of women registered for the period from January to December 2019 was downloaded from the RIC platform, each woman was given a folio, the resulting folios were printed and placed in a bag, the necessary folios were chosen until the sample was completed. From the selected folios, women aged 25 to 60 years, with

cervical cytology result and who had electronic clinical record in the Family Medicine Information System (FMIS) were included in the sample. The folios of women with no personal pathological history in the SIMF were excluded.

A history of chronic diseases in the FMIS was searched with the social security number. Overweight, obesity, diabetes, hypertension, human immunodeficiency virus and smoking habits, were considered when there was a record of these personal pathological antecedents in the medical history or medical note. The cervical cytology result was classified as normal when there was no presence of HPV or cellular atypia; low-grade intraepithelial lesion when there was presence of HPV and cervical intraepithelial neoplasia (CIN) 1; high-grade intraepithelial lesion with report of CIN 2, CIN 3 and cancer in situ.

Data entry was performed in Excel; the variables were folio, age, body mass index (BMI), hypertension, diabetes, HIV carrier, currently smoking and cervical cytology results. Statistical analysis was performed in SPSS v. 20. To establish the association, OR, 95% CI and p-value were calculated; logistic regression was performed for those variables that showed an association. This research did not require informed consent; the confidentiality of the obtained data was assured by including the initials of each woman and her social security number. The researchers who participated declared not having conflicts of interest. This protocol was submitted for evaluation to the Local Research and Ethics Committee and the Local Health Research Committee 1101, which is attached to the Family Medicine Unit No. 9.

Results

The minimum age of the participants was 25, with a maximum of 60, and a mean of 40 years (SD± 9). They had a minimum BMI of 19 kg/m², a maximum of 48 kg/m², with a mean of 29 (SD± 6). Overweight and obesity were the conditions with the highest frequency in the women who made up the sample, the descriptive analysis of chronic diseases is broken down in Table 1.

69.8% of women had a normal result (372/533), atypia, 3% (16/533), CIN 1, 17.4% (93/533), CIN 2, 5.6% (30/533), CIN 3, 3.4% (18/533) and cancer in situ, 0.8% (4/533).

The distribution of squamous intraepithelial lesions of the cervix and chronic diseases are presented based on the age of the woman, see Table 2.

The bivariate analysis showed a positive association of high-grade squamous intraepithelial lesion with age, diabetes, arterial hypertension, obesity, and smoking, see Table 3.

Backward binary logistic regression method found BMI and smoking as risk factors for the presence of intraepithelial lesion, see Table 4.

The variables age, diabetes, arterial hypertension, HIV, obesity and smoking were included in the model.

Discussion

In Paraguay,⁷ a study conducted in women aged 12 to 64 years from an indigenous population, 13.18% of intraepithelial lesions were found in cervical cytology reports; meanwhile, Solís et al.⁵ reported 4.49% incidence in

Table 1. Chronic Diseases in Women of the Sample

Chronic Disease	Coding	Frequency	Percentage %
Diabetes	Yes	77	14.4
	No	456	85.6
Systemic Arterial Hypertension	Yes	91	17.1
	No	442	82.9
Obesity	Obesity Class III	34	6.4
	Obesity Class II	56	10.5
	Obesity Class I	132	24.8
	Overweight	195	36.6
	Normal	116	21.8
HIV Carrier	Yes	4	0.8
	No	528	99.2
Smoker	Yes	49	9.2
	No	484	90.8

Table 2. Cervical Cytology and Chronic Diseases According Based on the Age

Variable		<40 years Frequency (%)	≥40 years Frequency (%)	Total Frequency (%)	P Value
Cervical Cytology Result	Normal	189 (65.6)	183 (74.7)	372 (69.8)	0.045
	Atypia	10 (3.5)	6 (2.4)	16 (3)	
	CIN 1	50 (17.4)	43 (17.6)	93 (17.4)	
	CIN 2	23 (8)	7 (2.9)	30 (5.6)	
	CIN 3	13 (4.5)	5 (2)	18 (3.4)	
	Cancer	3 (1)	1 (0.4)	4 (0.8)	
Diabetes	Yes	62 (21.5)	15 (6.1)	77 (14.4)	< 0.01
	No	226 (78.5)	230 (93.9)	456 (58.6)	
Systemic Arterial Hypertension	Yes	76 (26.4)	15 (6.1)	91 (17.1)	< 0.01
	No	212 (73.6)	230 (93.9)	442 (82.9)	
Obesity	Obesity Class III	22 (7.6)	12 (4.9)	34 (6.4)	0.016
	Obesity Class II	37 (12.8)	19 (7.8)	56 (10.5)	
	Obesity Class I	78 (27.1)	54 (22)	132 (24.8)	
	Overweight	101 (35.1)	94 (38.4)	195 (36.6)	
	Normal	50 (17.4)	66 (26.9)	116 (21.8)	
HIV Carrier	Yes	2 (0.8)	2 (0.8)	4 (0.8)	0.871
	No	286 (99.2)	243 (99.2)	529 (99.2)	
Smoker	Yes	28 (9.7)	21 (8.6)	49 (9.2)	0.64
	No	260 (90.3)	224 (91.4)	484 (90.8)	

Table 3. Bivariate Analysis of Chronic Disease and Cervical Cytology Result

Variable	Classification	High and Low Intraepithelial Lesion	Normal	OR	CI 95%	P value
Age	≥ 40 years	99	189	1.5	1.0-2.2	0.02
	25 a 39 years	62	183			
Type 2 Diabetes	Yes	31	46	1.6	1.0-2.7	0.03
	No	130	326			
Systemic Arterial Hypertension	Yes	36	55	1.6	1.0-2.6	0.03
	No	125	317			
Obesity	BMI ≥30	97	125	2.9	2.0-4.3	< 0.01
	BMI <30	64	247			
HIV	Yes	2	2	2.3	0.3-16.6	0.4
	No	159	370			
Smoker	Yes	26	23	2.9	1.6-5.2	< 0.01
	No	135	349			

women aged 21 to 64 years in a primary care unit; while Sánchez-Hernández et al.²² found 4.3% of cervical cytology results with intraepithelial lesions; this differs from the results of this research, in which 30.2% of the women presented an intraepithelial lesion; this difference can be explained by the age of the women and the size of the sample. The most frequent intraepithelial lesion in the present study was CIN 1, which is similar to that reported in other studies.^{5,7} A study carried out in Turkey showed a similar percentage to ours, with 30.3% of intraepithelial lesions in cervical cytology results, in which the most frequent was CIN 1.¹¹ Low-grade intraepithelial lesions are the most frequent, because most of them regress and do not evolve into a high-grade lesion.²⁶

Obesity is present in a large proportion of women who undergo cervical cytology; it has been reported in a study that 16.2% of the women had a BMI ≥30 and 52.5% were overweight; this differs from the results of this research, in which there was a predominance of obesity in 41.7% of the women.¹¹ Overweight and obesity have been associated as risk factors for numerous chronic diseases including diabetes, cardiovascular disease, and cancer; in a study in Egyptian women in 2016,²⁷ women with BMI >30 were found to be at increased risk for high-grade intraepithelial lesions (OR 5.42, 95% CI 3.03 to 9.74); which is consistent with what was found in this research. BMI represented a risk factor for the presence of intraepithelial lesions in cervix, however, in the research conducted by Kaplan et al.¹¹ a BMI >30 represented a protective factor (OR 0.6, 95% CI 0.42-0.97) for presenting intraepithelial lesions; these same findings were reported by Clarke

Table 4. Binary Logistic Regression of Chronic Diseases and Intraepithelial Lesion Result

Variable	OR	CI 95%	p value
Arterial Hypertension	1.08	0.63-1.8	0.75
Diabetes	1.15	0.66-2.0	0.6
HIV	0.54	0.06-4.3	0.56
Age	0.98	0.96-1.0	0.08
BMI*	1.3	1.1-1.5	< 0.01
Smoking	3.3	1.8-6.2	< 0.01

et al.¹³ who found that overweight and obese women in the cohort study had a lower risk of developing a premalignant lesion; however, obesity was associated with cervical cancer; the results regarding the relationship between obesity and squamous intraepithelial lesions of the cervix continue to diverge.

Chronic degenerative diseases such as arterial hypertension and diabetes are diseases of great health impact throughout the world, which have been associated with cancer; in this regard, it has been reported that suffering arterial hypertension (OR 4.5, 95% CI 1.6-12.9) is a risk factor for cervical cancer.²⁸ In a cohort study, an association was identified between having diabetes and developing urinary and digestive cancers;¹⁷ similar data have been reported in which diabetes was associated with pancreatic, liver, kidney, gallbladder and endometrial cancer.²⁰ In the present study, bivariate analysis found diabetes and arterial hypertension to be a risk factor for squamous intraepithelial lesions; however, in the logistic regression analysis, this association was not demonstrated.

The association between smoking and neoplasia has been described in several researches, scientific evidence

supports that smoking increases the risk of intraepithelial lesions and cervical cancer; a meta-analysis study in Japan reported that smokers had a higher risk of cervical cancer vs. to never smokers (OR 2.03, 95% CI 1.49 to 2.57).²⁹ In a meta-analysis by Plummer et al.,³⁰ a high risk of squamous cell carcinoma among active smokers was found (OR 2.03, 95% CI 1.49 to 2.57). In a meta-analysis by Plummer et al.,³⁰ it was found a high risk among cases of squamous cell carcinoma in active smokers (OR 2.30, 95% CI 1.31 to 4.04) and former smokers (OR 1.80, 95% CI 0.95 to 3.44). Kaplan found smoking to be a risk factor for developing intraepithelial lesions (OR 4.45, 95% CI 2.39 to 8.27).¹¹ Another meta-analysis study found a positive association between smoking and intraepithelial lesions (OR 1.67, 95% CI 1.37 to 2.04).²⁴ Other studies have reported similar results.^{22,23} These data are consistent with those obtained in the present investigation, which show that smoking was a risk factor for the presence of intraepithelial lesions.

HIV infection increases the risk of some malignant tumors, including cervix cancer; several studies have demonstrated that HIV-infected women are more likely than uninfected women to develop some type of neoplasia;³¹⁻³³ this is not consis-

tent with the results of this study, which found no association between HIV and intraepithelial lesions, more research is needed on the role of HIV in the presence of malignant tumors.

The scope of this research was to establish risk factors related to the development of cervical cancer and to have an overview of this problem and its possible approaches; from the point of view of the intervention, actions should be taken in primary care to control overweight and obesity as a health problem.

The limitations of this investigation were not to include other factors associated with cervical intraepithelial lesions, such as gynecological-obstetric history and previous reports of cervical cytology. In addition, the data were obtained from secondary sources of information such as the electronic clinical record and the RIC platform, women were not surveyed to identify the temporality of some variables such as smoking; somatometric measurements associated with obesity like abdominal perimeter, laboratory studies, as glycosylated hemoglobin, cholesterol, triglycerides and C-reactive protein, were not performed, which have been associated as predictors for developing high-grade intraepithelial lesions.

The sample was made up of individuals who attended a family medicine unit belonging to the Mexican Institute of Social Security, rather than the open population, therefore there was a sampling bias. The participants in our study do not belong to a representative sample of the Mexican population; it cannot be generalized to the entire population of the country. Further research is required and needs to be applied to the open population in rural and urban areas, with other types of social security.

Conclusion

In the present investigation, about one third of the women had intraepithelial lesions in the cervix, 32% (52/161) had high-grade intraepithelial lesions and the rest had low-grade lesions. Smoking and obesity were risk factors for the presence of low- and high-grade intraepithelial lesions.

The identification of chronic diseases that are risk factors for developing a neoplasm allows us to dimension the problem and the importance of promoting healthy lifestyles to improve individual and population health.

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