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Intraepithelial cervical lesions in indigenous in Ecuador

Lesiones intraepiteliales cervicales en indígenas del Ecuador

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Abstract

The aim of this research was to determine the prevalence of cervical intraepithelial lesions in indigenous women of Ecuador 2017. A descriptive study was performed. Population was formed by 2489 indigenous women aged 15 to 64 years old, of which 396 users were chosen by spontaneous demand. Frequency values and percentages were taken from qualitative variables, while mean and standard deviation were taken from quantitative variables. Prevalence of intraepithelial lesions was 13,8%. Average age was 31 years old. Uncertain importance's squamous atypical cells were higher in 30-to-39-year-old group (46,7%). Non-specific atypical glandular cells were observed in 66,7% of 30-to-39-year-old group. Low-grade intraepithelial lesions were majorly found in 20-to-29-year-old group (43,8%). High-grade intraepithelial lesions were also seen in 20-to-29-year-old group. Conclusions were: prevalence of intraepithelial lesions in indigenous women of Ecuador was higher than 10% of reported in other studies, and more frequent in those aged 20 and 39 years old.

Keywords: Uterine cervical dysplasia, cervix neoplasms, intraepithelial cervical neoplasm

Resumen

El objetivo de esta investigación fue determinar la prevalencia de lesiones intraepiteliales cervicales en mujeres indígenas del Ecuador 2017. Se realizó un estudio descriptivo. La población estuvo compuesta por 2489 mujeres indígenas de 15 a 64 años, de las cuales 396 usuarias fueron elegidas por demanda espontánea. De las variables cualitativas se obtuvieron los valores de frecuencia y porcentajes, y de las cuantitativas la media y la desviación estándar. La prevalencia de las lesiones intraepiteliales fue del 13,8%. La edad promedio fue 31 años. Las células escamosas atípicas de importancia incierta fueron mayores en el grupo de edad de 30 a 39 años (46,7%). Se observaron células atípicas glandulares no específicas en el 66,7% en el grupo de 30 y 39 años de edad. Las lesiones intraepiteliales de bajo grado se presentaron más en el grupo de 20 y 29 años (43,8%). Las lesiones intraepiteliales de alto grado se identificaron también en el grupo de 20 a 29 años de edad. Las conclusiones fueron: la prevalencia de lesiones intraepiteliales en las mujeres indígenas del Ecuador fue superior al 10% de las reportadas en otros estudios, y más frecuente en aquellas de 20 y 39 años de edad.

Palabras clave: displasia cervical uterina, neoplasias del cuello uterino, neoplasia intraepitelial cervical.

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Introduction

According to the Center for Disease Control and Prevention (CDC), between 50 and 75% of sexually active adults will be hosts to the human papilloma virus at some point in their lives. Globally, an estimated of 291 million women worldwide are carriers of Human Papilloma Virus (HPV) (1).

In the countries of Latin America, the prevalence data of cytologic alterations are very variable and are taken in restricted population groups, such as Mexico with 3.4%, Venezuela 13.2% and Ecuador 9.8%. In Paraguay the screening with cervical-vaginal cytology does not exceed 10%; In a study with 5,712 cytologies performed in Spain, a total amount of 308 (5.4%) cervical epithelial abnormalities were found. On the other hand, in the United States of America this alteration is found in different studies between 7 and 23% (2).

Cervical cancer (CC) is the third leading cause of death among women worldwide, with an estimated overall mortality rate of 15 per 100,000 women. CC was the second most common cause of death in Mexican women in 2011 (10.4%). The immune system plays a key role during HPV-associated carcinogenesis, as HPV elimination is determined by specific immunological reactions. Therefore, CC appears to be due in part to a failure of the immune system that is unable to eliminate persistent HPV infections and virus-transformed cells (3).

It is now understood that human papillomavirus (HPV) infection is a major cause of cervical cancer, but only a minor fraction of all HPV infection progresses to precancerous lesions and cancer. There are more than 200 different HPV genotypes that are classified as high risk (HR) and low risk (LR). High-risk strains are most frequently found in HPV 16, 18 and 45 (4).

Intraepithelial lesions may progress to cervical uterine cancer; being this pathology the third cause of cancer death in women worldwide and the second one in Ecuador. The odds of developing cervical cancer according to the Sociedad de Lucha Contra el Cáncer (SOLCA) are 2% at 39 years, 9% at 50 years, and 23% at 79 years; with a crude rate of 36.5% and with 6% annual mortality (5).

Regarding cancer in women, breast cancer is the first and cervical the second, being the fourth leading cause of death in female population worldwide, with an approximate 528,000 new cases and 266,000 deaths per year. 85% of cases occur in developing countries. The incidence of CC in Ecuador in 2014 was 2094 new cases, and is the second cause of death with a risk of 14.4% (6).

According to the national tumor registry of SOLCA-Quito, the incidence in 2013 was 15.8 cases per 100,000 inhabitants. The Instituto Nacional de Estadística y Censos (INEC) in 2015, and with the classification of ICD-10, describes the cervical cancer as: malignant tumor in the cervix with a report of 10 cases (6.7%); malignant tumor in the cervix without other specification: 1345 (6.9%);

carcinoma in situ in the cervix: 2 (8.6%); carcinoma in situ in the cervix, non-specific part: 234 (8.7%) (7).

One of the main causes of death in women in Ecuador is cervical cancer. According to statistics, it is the second leading cause of death in women over 35 (8).

Cabrera V et al (9), carried out a study to determine HPV subtypes in 500 women of reproductive age and from the parishes of the Cuenca canton. The genes found for cervical cancer were: 51, 16, 66, 5, 35, 39, 58, 68, 18, 31, 56, 33, 45 and for genital warts: 42, 43, 6, 11, 44 (10).

Among the main factors that cause intraepithelial lesions that lead to cervical cancer induced by HPV infection are: age, alcoholic beverages intake, tobacco, early onset of sexual intercourse, high number of sexual partners, prolonged use of oral contraceptives, cervical trauma during labor, endogenous genetic and hormonal factors associated with pregnancy (11).

Method

Research Design: non-experimental.

Study Type: descriptive, cross-sectional.

Study Universe: the universe was constituted by the female population with indigenous self-identification of Quilloac (Kañari), Saraguro (Saraguro) and Macas (Shwuara) according to the Instituto Nacional de Estadística y Censos (INEC) of 2010: 2489 (12).

Sample size calculation: The sample size was calculated with a prevalence for intraepithelial lesions of 10.2%; with a confidence level of 95%, an error margin of 3%, considering a total population of 2489 Indians and, analyzing the possibility of a 10% loss.

Finally, the study was performed in 396 women aged 15-64 who met the inclusion and exclusion criteria; the selection of patients was by stratified probabilistic sampling.

Inclusion Criteria:

- Indigenous with sexual activity background.
- 15-to-64-year-old age.
- Last sexual intercourse \geq to 3 days.
- Signing of informed consent.

Exclusion Criteria:

- Transvaginal bleeding (menstruation)
- Abundant pathological vaginal secretion.
- Previous use (< 48 hours) of vaginal douche, ovules, jellies.
- Pregnancy.

Methodology: to obtain cervical cellularity, liquid cytology technique (ThinPrep-Paptest) was applied; personnel training for the collection of sociodemographic data was previously performed; and for the collection of biological samples with the ThinPrep-Paptest (TPPT) technique, liquid-based cytology was done; this training was handled by physicians specializing in the gynecology and pathology areas to doctors at health centers.

Cervical sample collection was obtained through a TPPT, a food tool approved by the FDA (Food and Drug Administration) "significantly more effective" than the conventional technique for detecting cervical lesions including improved detection of glandular lesions, since it allows an optimized collection of cervical cellularity reducing false negatives. The sample collected by the broom device is placed in a bottle with a fixative liquid and then sent to the laboratory where the cells will be homogenized by the agitation method or centrifugation that will later be deposited in the slide, framed within a technical processing automated (13).

As stated in the study, a form was designed, in which the variables to be studied were collected in a concrete way.

Ethical aspects: this research was carried out using the principles of the laws and regulations of the country that underpin the greatest protection to the individual and the Declaration of Helsinki, adopted by the 6th General Assembly, Fortaleza, Brazil, October 2013 (14). Therefore, this study for its execution Received the approval of the Bioethics Committee of the School of Medical Sciences of the Universidad de Cuenca; in this framework and prior to data collection, community leaders were informed: the project aims the confidentiality of the data, the desire to withdraw at any time, the adverse effects of taking the biological samples and the characteristics of health personnel; after their acceptance the participants signed the informed consent.

Statistical Analysis; depending on the type of variable and for the purpose of summarizing the information, we worked on the quantitative variables with the arithmetic mean (\bar{x}) and standard deviation; for qualitative variables with frequencies (N°) and percentages (%).

Result

The average relative to the age of the users who participated in the study was 31 years; The Body Mass Index (BMI): 27 Kg/m²; the number of gestations: 3; the number of births: 2; the mean age of the first birth was 18 years; In relation to beginning of active sex life: average was 16 years (Table 1)

Of the 55 users diagnosed with intraepithelial lesions in the uterine cervix: 15.8% (23) were of Shwara ethnicity, followed by Saraguro in 14.9% (18), and 14.7% (25) were married, 16.4% (25) had a primary education level (Table 2).

The diagnosis of intraepithelial lesions of the cervix using the TPPT system was 55 cases, with a prevalence of 13.8% (Table 3).

Table 1. Distribution according to age, body mass index and obstetric background, in indigenous women from Cañar, Saraguro and Macas; 2016.

Variable	Media	Standard deviation	Number of participants
Age	31	8.5	396
Body mass index	27	4.0	396
Number of pregnancies	3.1	2.1	396
Number of births	2.7	1.9	396
Number of abortions	0.3	0.7	396
First birth age	18	5.7	396
Start of active sexual life	16.8	2.8	396

Table 2. Distribution according to intraepithelial lesion diagnosis by ethnic group, residence, marital status, education level, of indigenous women from Cañar, Saraguro and Macas; 2016.

Variables		Intraepithelial lesion diagnosis			
		Yes		No	
		n	%	n	%
Ethnic group	Kañari	14	10,7	117	89,3
	Shwara	23	15,8	123	84,2
	Saraguro	18	14,9	103	85,1
Residence	Cañar	14	10,7	117	89,3
	Macas	23	15,8	123	84,2
	Saraguro	18	14,9	103	85,1
Marital Status	Single	9	12,9	61	87,1
	Consensual Union	15	10,6	127	89,4
	Married	25	14,7	145	85,3
	Divorced	3	50,0	3	50,0
	Widow	3	30,0	7	70,0
Education Level	No answer	0	0,0	2	100,0
	None	0	0,0	5	100,0
	Literacy Center	2	15,4	11	84,6
	Elementary	25	16,4	127	83,6
	High School	22	11,9	163	88,1
	Third level	2	6,3	30	93,8
Fourth level	4	44,4	5	55,6	

N: recount; %: porcentaje

Table 3. Prevalence of intraepithelial lesions, according to number of diagnosed cases, in indigenous women from Cañar, Saraguro and Macas; 2016.

		Intraepithelial Lesions	
		Frequency	Percentage
Cases	yes	55	13,8
	no	341	86,2
Total		396	100,0

Regarding intraepithelial lesions, atypical squamous cells of uncertain significance (ASC-US) were more frequent in the 30-to-39-year-old age group: 14 cases (46.7%), in the older-than-40 year-old group: 7 (23.3%), in the 20-to-29-year-old group: 7 (23.3%); And 2 cases in the less-than-20-year-old group (6.7%). Non-specific glandular cell atypia (ACG-NOS) was observed in 66.7% (2) in women aged 30 and 39 years old, and 1 (33.3%) in the population aged 20 and 29 years old; low-grade squamous intraepithelial lesions (LSIL), were present in the highest number in the 20-and-29-year-old group: 7 (43.8%), and 6 (37.5%) in the 30-and-39-year-old group; And only 3 (18.8) cases in the older 40-than-year-old group. High grade squamous intraepithelial lesions (HSIL) were diagnosed equally in the 20-to-29 and 30-to-39 years old age groups, there were no cases in the over-than-40-year-old group (Table 4 and Figure 1).

Table 4. Distribution according to Intraepithelial-lesion diagnosis by age groups, in indigenous women from Cañar, Saraguro and Macas; 2016.

Intraepithelial-lesion		< 20 years	20 to 29 years	30 to 39 years	> 40 years
		n (%)	n (%)	n (%)	n (%)
ASC-US	Yes	2 (6,7)	7 (23,3)	14 (46,7)	7 (23,3)
	No	31 (8,5)	140 (38,3)	132 (36,1)	63 (17,2)
ACG-NOS	Yes	0 (0,0)	1 (33,3)	2 (66,7)	0 (0,0)
	No	33 (8,4)	146 (37,2)	144 (36,6)	70 (17,8)
LSIL	Yes	0 (0,0)	7 (43,8)	6 (37,5)	3 (18,8)
	No	33 (8,7)	140 (36,8)	140 (36,8)	67 (17,6)
HSIL	Yes	0 (0,0)	3 (50,0)	3 (50,0)	0 (0,0)
	No	33 (8,5)	144 (36,9)	143 (36,7)	70 (17,9)

ASC-US: atypical squamous cells of uncertain significance; ACG-NOS: non-specific glandular cell atypia; LSIL: low-grade squamous intraepithelial lesions; HSIL: high-grade squamous intraepithelial lesions.

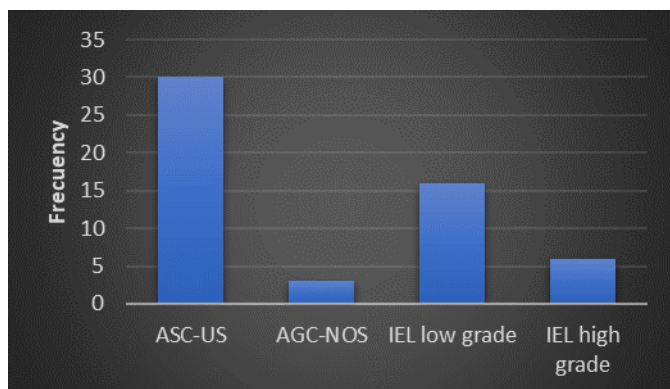


Figure 1. Intraepithelial lesions type, according to number of diagnosed cases, in indigenous women from Cañar, Saraguro and Macas; 2016.

ASC-US: atypical squamous cells of uncertain significance; ACG-NOS: non-specific glandular cell atypia; IEL: intraepithelial lesion.

Discussion

The ages of users who participated in the study were mostly between the ages of 33 and 34 years old. In the study by Hernández et al. (15), in which they analyzed 2222 results of cervical cytology, they observed in patients an average age of 38 years old; all diagnoses of intraepithelial lesions were determined by the Bethesda system, where the sample was represented mostly by ASC-US (62 cases), and low-grade intraepithelial lesions with 27 cases. These results coincide with the investigation where the highest number of lesions observed were ASC-US being 30 cases, and 16 cases of low-grade intraepithelial lesions in 396 patients.

The Shwara ethnic group had a participation frequency of 36.7%; 46.5% had a secondary level of education; 42.7% had a consensual union marital status. Users who were diagnosed with cervical intraepithelial lesion had a diagnosis of overweight, according to their nutritional status, determined by BMI and World Health Organization's criteria in 193 participants.

During the investigation, using the ThinPrep-Paptest system, the diagnosis of intraepithelial lesion of the cervix was observed in 55 cases, with a prevalence of 13.8% for the sample of 396 indigenous women in the area 6. In the study by Mendoza T (16), in a universe of 3,539 women, the prevalence of IEL found was 12.5%. Compared with Nuñez M (17), the prevalence of intraepithelial lesions in women aged 30 and 49 years old was 11.2%.

Armenteros, E et al. (18), observed 34 women diagnosed with intraepithelial lesion and 64 without diagnosis, determined that the onset of active sexual life before age 15 was a risk factor for acquiring this pathology.

Trujillo E (19); analyzed 543 pathological cytologies in women with ages between 19 and 75 years old, the majority in the 37-year-old age; the reported results were: 35.2% for ASC-US; 43.5% low-grade intraepithelial lesion; 21.4% high grade intraepithelial lesion. The genotypes related to these cytological alterations were 16 and 58.

In the research performed by Mercado-Gutierrez MR et al. (20), out of a total of 67,935 Paptest for four years, cytological samples with diagnosis of LSIL, HSIL were twice as high in women younger-than-35 years old (6.5 vs. 3.7%). 88.8% of HSIL was associated with HR-HPV 16, which increases the likelihood of HSIL against LSIL regardless of age.

In relation to intraepithelial lesions, we observed: 7.8% of ASC-US, and more frequent in the 30-to-39-year-old age group: 14 cases (46.7%); In the older-than-40-year-old group: 7 (23.3%); In the group of 20 and 29 years old: 7 (23.3%); And in less-than-20-year-old group: 2 cases (6.7%). 0.8% ACG-NOS: in 66.7% (2) in women aged 30 and 39 years old, and 1 (33.3%) in the population aged 20 and 29 years old. 4% low-grade intraepithelial lesion: in the 20 and 29 years old 7 (43.8%); 6 (37.5%) in the 30 and 39 years old; and only 3 (18.8%) cases in the older-than-40-year-old group. This research differs with the study by Cabrera V et

al. (2) in 500 patients that reported a prevalence of ASC-US of 7% and intraepithelial lesion of low grade 1.8%; And by age group they obtained ASC-US: 20 to 29 years old 0.8%; 30 to 39 years old 2.8%; And in those older than 40 years old, 3.4% and intraepithelial lesion under 0.6% for all 3 groups. The study by Banegas G et al. (21), in 146 users, found, on the other hand, a prevalence for ASC-US of 8.2%.

Solis and Briones, (22) in 2018, in a Instituto de Seguridad Social de México's 379-patient sample, found a 42.8-year-old (DS 10.4) age average. Cervix intraepithelial lesions' prevalence was 4.49% (n 17); of which 3.17% (n 12) were low-grade IEL, and 1.32% (n 5) were high-grade IEL; carcinoma was not observed in studied patients' cytology reports. These data differ from the data found in this research, where IEL prevalence was higher.

Velazquez C, et al. (23) in 2018, in a Paraguay's 129-indigenous-women population, reported a 13.18% IEL prevalence, the major age group was 25-to-44 years old (70.59%); menarche's average age was less than 12 years old; 76.5% had their start of sexual life before 15 years old; and 82.35% of participants had more than 5 children. IEL's most frequent findings were: ASC-US 10.08%, Type I cervical intraepithelial neoplasms (NIC I) 2.32%; NIC II 0.77%; NIC III nor carcinoma in situ were not observed. These data relate with our indigenous population's.

Galucho D, (24) in his thesis titled "Prevalence of cervix intraepithelial lesion assessed by Paptest and cervix biopsy in Alfredo Noboa Montenegro Hospital's gynecology external consultation service"; in a 78-cytology sample, where the major average age group were 40-to-50-year-old women (39.8%). 60.2% of patients had a normal Paptest result, while 39.7% had a pathological result, of which 27.7% were NIC I, 6% NIC II, 3.6% NIC III, 1.2% belong to NIC IV and cancer in situ. Prevalence, which differs even with reported as general in literature.

Carrion J, (25) in 2019, in his transversal-analytical type research, performed in a Cañar-Ecuador's indigenous population; found out in a 100-Kañari-Ethnic-group's-women sample, aged 15 and 55 years old, a 2%-intraepithelial-cervical-lesion frequency, as a result from conventional-cytology reports. Besides, 34% had a positive result for HPV in his group, being genotype 31 the frequent (41.2%), followed by genotype 16 in 20.6% of cases. This prevalence in much lower than this study.

In the study conducted by the University Hospital Thammasat, July 2013-2016, performed by Reyes Albarrán JM et al, (26), where cervical screening was performed in a total of 2,144 users using the liquid cytology technique, using the terminology of the Bethesda 2001 system (27) for the interpretation of the results, the results obtained were: the age of both groups was not statistically significant difference in $p = 0.109$. There were more cases of abnormal cytology mostly as ASC-US; in patients with LSIL, there were 22 cases.

Conflict of interests

The authors have no conflicts of interest to disclose.

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STZK and CHFR: statistical analysis and biological sampling. **MBMR:** histopathologic analysis and bibliographic review. **CRBS and SSGM:** bibliographic review.