# Risk factors associated with cervical dysplasia in women treated in a Peruvian hospital

## Factores de riesgo asociados a la displasia cervical en mujeres atendidas en un hospital peruano

Jorge Ybaseta-Medina[1]

**ABSTRACT**

**Objective:** To identify risk factors associated with cervical dysplasia in women older than 17 years. **Methods:** Case-control investigation involving 105 women (35 cases and 70 controls) in a regional hospital during the period January-December 2018. The information was obtained from medical records, entered into the Epi Data version 4.6 and exported to SPSS version 26 for study. Multivariate logistic regression analysis was performed, calculating odds ratios (OR) and 95% confidence intervals (95% CI). A value of $p < 0.05$ was considered statistically significant. **Results:** Risk factors for cervical dysplasia were identified as secondary educational status or lower (ORa = 17.2, 95% CI 1.7-176.5), number of partners greater than three (ORa = 11.7, 95% CI 1.5-94.9), multigestation (ORa = 17.9, 95% CI 1.1-29.6) and use of oral contraceptives (ORa = 318.3, 95% CI 5.6-171.7). **Conclusion:** Secondary education or less, number of partners greater than 3, being multigestational, and oral contraceptive use were associated with an increased likelihood of having cervical dysplasia. Interventions should be made to strengthen health education on sexual practices with information on the desirability of early detection of cervical dysplasia.
**Key words:** Human papillomavirus 16, Risk factors, Multiple sexual partners, Squamous intraepithelial lesions

**RESUMEN**

**Objetivo.** Identificar los factores de riesgo asociados a la displasia cervical en mujeres mayores de 17 años. **Métodos.** Investigación de casos y controles con la participación de 105 mujeres (35 casos y 70 controles) en un hospital regional durante el periodo de enero a diciembre de 2018. La información se obtuvo de expedientes médicos, fue ingresada al programa Epi Data versión 4.6 y exportada al SPSS versión 26 para su estudio. Se realizó un análisis de regresión logística multivariante, calculándose los *odds ratio* (OR) y los intervalos de confianza al 95% (IC 95%). Se consideró estadísticamente significativo un valor de $p < 0,05$. **Resultados.** Se identificó como factores de riesgo para displasia cervical al estadio educativo secundaria o inferior (ORa = 17,2, IC 95%: 1,7 a 176,5), número de parejas mayor a tres (ORa = 11,7, IC 95%: 1,5 a 94,9), ser multigesta (ORa = 17,9, IC 95%: 1,1 a 29,6) y usar anticonceptivos orales (ORa = 318,3, IC 95%: 5,6 a 171,7). **Conclusión.** El grado de instrucción secundaria o inferior, el número de parejas mayor a 3, ser multigesta y el uso de anticonceptivos orales se relacionaron a una mayor probabilidad de portar displasia cervical. Se deben realizar intervenciones para fortalecer la educación sanitaria sobre las prácticas sexuales con información sobre lo conveniente de la detección temprana de la displasia de cérvix.
**Palabras clave.** Virus del papiloma humano 16, Factores de riesgo, Parejas sexuales múltiples, Lesiones intraepiteliales escamosas

## INTRODUCTION

Cervical cancer (UCC) is a slowly progressive neoplasm that begins in the superficial cells of the cervix[1,2] with atypical changes known as cervical dysplasia. These dysplastic cells are precancerous and gradually progress to cervical intraepithelial neoplasia[3-5].

The World Health Organization reports that cervical cancer ranks fourth in the world in affecting women, with an incidence rate of 13.3% and a mortality rate of 7.3 per 100,000 women. Furthermore, globally it is considered the second most recurrent neoplasm affecting women between 20-69 years of age, with an incidence of 22.8 per 100,000 women in Latin America[3,6].

One of the challenges proposed in the Sustainable Development Goals is to address the lack of access to early diagnosis and effective and appropriate treatment for cervical cancer. Due to inefficient screening programs, women tend to be diagnosed at advanced stages of the disease, at which point curative treatment is no longer a viable option[6].

Despite the implementation of various screening methods for UCC, in most countries[1] there are still limitations in the supply of services for histopathological diagnosis and accessibility to treatment, especially in developing countries, resulting in high mortality rates[6].

UCC progresses gradually. Human papillomavirus (HPV) infection has been identified as an important factor leading to cervical cancer, although HPV infection alone cannot cause the disease. With persistent HPV infection, decades are required for progression to cervical cancer and the ability to become invasive cancer if not detected and treated promptly[7]. This extended window of time provides a golden opportunity for clinical intervention[5]. It has been noted that immunosuppressed individuals are more likely to have recurrent HPV infections and experience more rapid progression to cancer[8].

UCC is easily preventable with proper universal application of the Papanicolaou smear (Pap), which has allowed early detection and timely treatment of precancerous lesions. However, it remains a common genital cancer in clinical practice in low-income women without access to tests with greater diagnostic value[9].

Studies indicate that the presence of HPV is significantly higher in women aged 15-24 years (OR: 1.48; 95% CI: 1.01-2.18), with a higher number of sexual partners (OR: 2.94; 95% CI: 1.23-7.02) and with coital relations before the age of 17 years (OR: 1.39; 95% CI: 0.64-3.06)[10-12].

Factors that condition HPV infection, its persistence and progression from cervical dysplasia to invasive cervical cancer include early onset of coital activity, multiple sexual partners or partners with multiple sexual partners and others, such as smoking, high parity and mixing with other sexually transmitted pathologies[12-14].

In developing regions, cervical cancer remains a major threat to women's health. It is essential to identify those with risk factors, implement screening programs and perform screening sequentially to reduce the morbidity and mortality associated with this disease. The screening process may include performing a Papanicolaou test to assess the degrees of dysplasia in cervical cells, which can be complemented by colposcopy and biopsy when necessary[6,7,11,12].

The result of the present study can serve as a complement to the regional and national guideline by providing information to health authorities to take appropriate measures[1]. The magnitude of risk factors associated with cervical dysplasia in women attending a referral hospital in southern Peru is evaluated.

## METHODS

This study is epidemiological in nature and adopts a case-control analytical design. It was conducted in women who received care at the Hospital Regional de Ica (HRI), Peru, during 2018. This hospital is positioned as a referral center in the Ica region, as well as in nearby provinces that are part of the Ayacucho and Huancavelica regions. The HRI offers medical services to the resident population of these specific areas.

The cases were characterized by presenting cervical dysplasia after Pap, colposcopy and biopsy. Cases were obtained by accessing medical records, Pap reports and histological result with high-grade intraepithelial lesion (HSIL). Controls were women seen in the gynecology service with negative Pap examination. The ratio of the number of cases and controls was two women with normal Pap results as controls for each woman diagnosed with cervical dysplasia.

Cases were included for women aged 17-64 years with histologic findings of HSIL and complete clinical history. The controls were the same age group, with complete clinical history and two negative annual Pap tests.

The population was 1,002 patients with Pap examinations, the sample size was 105, being 35 cases with histological result of HSIL and 70 controls that met the inclusion criteria.

Data were collected mainly from the respective medical records, as well as from the record book of the pathology service of the HRI. The data were recorded in a data collection form specially designed for this work. The study variables were sociodemographic, sexually transmitted disease, contraceptive methods and harmful habits. The validity of the instrument was through a validation form, which was provided to five experts made up of obstetrician-gynecologists and teachers who teach research methodology.

After the information was collected, the data were classified and a matrix was made from all the collection forms. The data were checked, coded, entered into EPI Data version 4.6 and finally exported to SPSS version 26 for analysis. The statistical analysis described the qualitative variables using frequencies and percentages. In the bivariate analysis, the nonparametric chi-square statistic was used to evaluate the statistical association between qualitative variables. Odds ratios with their corresponding 95% CIs were used to measure risk, considering that an OR value > 1 establishes the risk of developing cervical dysplasia. A multivariate analysis through logistic regression was also included. A $p$-value < 0.05 was considered significant.

In order to protect the confidentiality of the participating patients, codes were assigned to the clinical histories included in the study. The research protocol was registered and received authorization from the Institutional Ethics and Research Committee of the Regional Hospital of Ica.

## RESULTS

Of 1,002 Pap smears recorded in the anatomic pathology department of the HRI, 10% were identified as having HSIL.

In the sample of 35 cases and 70 controls it was found that having a secondary or lower educational status was an important risk factor: cases were more than four times more likely to have disease than controls (Table 1).

No significant statistical association was demonstrated between the risk groups for sexually transmitted disease and cervical dysplasia (Table 2). However, having had more than three partners increased the risk of cervical dysplasia twofold.

Table 3 shows that being multigestational increases the probability of suffering cervical dysplasia 13 times. Table 4 reveals that alcohol intake increases 11 times the likelihood of cervical dysplasia compared to those who do not consume alcohol. Table 5 shows that secondary or lower educational status, having more than three sexual partners, being multigestational and the use of oral contraception are associated with the presence of cervical dysplasia.

## DISCUSSION

Cervical neoplasia represents a pending public health problem for high and low-income nations. Globally, the high mortality rate from cervical cancer could be reduced by a comprehensive approach, including prevention, identification of risk factors, early detection, and effective treatment[15,16]. The identification of associated factors for precancerous cervical lesions is relevant for policy makers to develop preventive strategies.

The frequency of cervical dysplasia has been found to be 10%, lower than the 13.8% in Paraguay[17] and African countries, where it ranges from 1% to 27%[18,19]. These discrepancies may be

TABLE 1. SOCIODEMOGRAPHIC FACTORS FOR THE PRESENCE OF CERVICAL DYSPLASIA.

| | | Case | | Control | | OR | IC95% | | p |
|---|---|---|---|---|---|---|---|---|---|
| | | n | % | n | % | | Lower | Upper | |
| Age | <35 years | 8 | 22.9 | 44 | 62.9 | 0.175 | 0.069 | 0.442 | 0 |
| | ≥ 35 years | 27 | 77.1 | 26 | 37.1 | | | | |
| Educational status | Elementary to high school | 27 | 77.1 | 30 | 42.9 | 4.5 | 1.793 | 11.293 | 0.001 |
| | Higher education | 8 | 22.9 | 40 | 57.1 | | | | |
| Marital status | Engaged | 18 | 51.4 | 36 | 51.4 | 1 | 0.444 | 2.252 | 1.000 |
| | Single | 17 | 48.6 | 34 | 48.6 | | | | |
| Origins | Rural | 10 | 28.6 | 24 | 34.3 | 0.767 | 0.317 | 1.856 | 0.767 |
| | Urban | 25 | 71.4 | 46 | 65.7 | | | | |

OR: odds ratio, IC: confidence interval, p: chi square

TABLE 2. FACTORS RELATED TO SEXUALLY TRANSMITTED DISEASE ACCORDING TO THE PRESENCE OF CERVICAL DYSPLASIA.

| | | Case | | Control | | OR | IC95% | | p |
|---|---|---|---|---|---|---|---|---|---|
| | | n | % | n | % | | Lower | Upper | |
| Age of first sexual intercourse | <17 years | 14 | 40.0 | 26 | 37.1 | 1.128 | 0.491 | 2.593 | 0.776 |
| | ≥17 years | 21 | 60.0 | 44 | 62.9 | | | | |
| Number of sexual partners | >3 | 22 | 62.9 | 32 | 45.7 | 2.01 | 0.875 | 4.615 | 0.098 |
| | ≤3 | 13 | 37.1 | 38 | 54.3 | | | | |
| Urinary tract infection | Yes | 8 | 22.9 | 11 | 15.7 | 1.589 | 0.574 | 4.399 | 0.37 |
| | No | 27 | 77.1 | 59 | 84.3 | | | | |
| Trichomoniasis infection | Yes | 1 | 2.9 | 5 | 7.1 | 0.382 | 0.043 | 3.405 | 0.372 |
| | No | 34 | 97.1 | 65 | 92.9 | | | | |
| Condyloma infection | Yes | 3 | 8.6 | 5 | 7.1 | 1.219 | 0.274 | 5.422 | 0.795 |
| | No | 32 | 91.4 | 65 | 92.9 | | | | |
| Bacterial vaginosis | Yes | 5 | 14.3 | 5 | 7.1 | 2.167 | 0.583 | 8.053 | 0.24 |
| | No | 30 | 85.7 | 65 | 92.9 | | | | |
| Gonorrhea infection | Yes | 1 | 2.9 | 1 | 1.4 | 2.029 | 0.123 | 33.442 | 0.614 |
| | No | 34 | 97.1 | 69 | 98.6 | | | | |

OR: odds ratio, IC: confidence interval, p: chi square

TABLE 3. REPRODUCTIVE AND CONTRACEPTIVE-RELATED RISK FACTORS FOR THE PRESENCE OF CERVICAL DYSPLASIA.

| | | Case | | Control | | OR | IC 95% | | p |
|---|---|---|---|---|---|---|---|---|---|
| | | n | % | n | % | | Lower | Upper | |
| Number of pregnancies | Multigravida | 16 | 45.7 | 4 | 5.7 | 13.985 | 4.149 | 46.533 | 0.000 |
| | Primigravida | 19 | 54.3 | 66 | 94.3 | | | | |
| Parity | ≥ 2 births | 27 | 77.1 | 45 | 64.3 | 1.875 | 0.741 | 4.743 | 0.181 |
| | 1 birth | 8 | 22.9 | 25 | 35.7 | | | | |
| Use of oral contraceptives | Yes | 23 | 65.7 | 36 | 51.4 | 1.81 | 0.781 | 4.196 | 0.164 |
| | No | 12 | 34.3 | 34 | 48.6 | | | | |
| Rhythm method | Yes | 13 | 37.1 | 36 | 51.4 | 0.558 | 0.243 | 1.281 | 0.167 |
| | No | 22 | 62.9 | 34 | 48.6 | | | | |
| Use of injectable | Yes | 7 | 20 | 36 | 51.4 | 0.236 | 0.091 | 0.612 | 0.002 |
| | No | 28 | 80 | 34 | 48.6 | | | | |
| Use of IUD | Yes | 5 | 14.3 | 38 | 54.3 | 0.14 | 0.049 | 0.404 | 0 |
| | No | 30 | 85.7 | 32 | 45.7 | | | | |

OR: odds ratio, IC: confidence interval, p: chi square, IUD: intrauterine device

TABLE 4. FACTORS LINKED TO HARMFUL HABITS FOR THE PRESENCE OF CERVICAL DYSPLASIA.

| | | Case | | Control | | OR | IC95% | | p |
|---|---|---|---|---|---|---|---|---|---|
| | | n | % | n | % | | Lower | Upper | |
| Tobacco consumption | Yes | 0 | 0 | 3 | 4.3 | - | - | | 0.214 |
| | No | 35 | 100 | 67 | 95.7 | | | | |
| Alcohol consumption | Yes | 14 | 40 | 4 | 5.7 | 11 | 3.264 | 37.068 | 0 |
| | No | 21 | 60 | 66 | 94.3 | | | | |
| Drug consumption | Yes | 1 | 2.9 | 1 | 1.4 | 2.029 | 0.123 | 33.442 | 0.614 |
| | No | 34 | 97.1 | 69 | 98.6 | | | | |

OR: odds ratio, IC: confidence interval, p: chi square

due to differences in the skills of the test providers, study period, age of the populations studied and the underlying presence of sexually transmitted infections.

The study revealed that there are sociodemographic risk factors related to dysplasia, including marital status with a partner, level of education and coming from an urban area.

Regarding marital status with a partner, the frequency coincides with the result found in Mexico by Galván et al.[20] and differs from other studies[21,22] which report that the single factor has

TABLE 5. MULTIVARIATE ANALYSIS OF ASSOCIATED FACTORS ACCORDING TO THE PRESENCE OF CERVICAL DYSPLASIA. OF CERVICAL DYSPLASIA.

| | p value | OR | IC 95% | |
| --- | --- | --- | --- | --- |
| | | | Lower | Upper |
| Secondary to lower educational status | 0.017 | 17.2 | 1.7 | 176.5 |
| >3 sexual partners | 0.021 | 11.7 | 1.5 | 94.9 |
| Multigesta | 0.044 | 17.9 | 1.1 | 29.6 |
| Use of oral contraceptives | 0.005 | 318.3 | 5.6 | 171.7 |
| Use of injectables | 0.003 | 0.1 | 0 | 0.3 |
| Use of IUD | 0.001 | 0.1 | 0 | 0.1 |

OR: odds ratio, IC: confidence interval, p: chi square

increased in the majority of neoplasms, which may be due to the increase in single women, with no association between cervical dysplasia and marital status.

The level of secondary education or lower was statistically significant (Table 5), in agreement with studies by Thakur A et al.[3] and Legasu T et al[23]. Illiterate or less educated individuals are prone to less information; hence it is possible that individuals with low educational level are unaware of the development of the disease and the importance of Pap smear[3,14].

In the study, having 3 or more sexual partners would increase the probability of precancerous lesion of the cervix by 11.7 times, a result greater than that found by Tsehay B et al.[11], Abarca et al.[24] and Sequera et al.[25] of 2 times the possibility of risk of cervical dysplasia in Ethiopia, Costa Rica and Uruguay, respectively. Several studies support that having more than 3 or more sexual partners is a significant associated factor for HPV infection, which is the etiological agent of cervical dysplasia and cervical cancer[11,13,18,21,26].

The study showed that being multigestational increases 17 times the risk of having cervical dysplasia. Other researchers such as Conde[14] and Galván[20] found an association between a history of multiple pregnancies and high-grade squamous intraepithelial lesions. This result would depend on the presence of other factors, such as the number of partners, promiscuity, decreased immunity and mainly pathology in sexual transmission.

The use of oral contraception as a predisposing factor for cervical dysplasia coincides with other studies[2,27-30], which would be explained because the hormonal increase would cause some cells to multiply more than normal and there would be more susceptibility of cervical cells to persistent infection of high-risk HPV[20,25].

The limitations of the study include the fact that it is a single center, with source of information from clinical records and lack of quality information, mainly in history, origin, and diagnoses. Like other case-control studies, it is subject to selection bias and the possibility that the cases and controls were not representative of the population studied.

## CONCLUSION

We found that having a high school education or lower, more than three sexual partners, multigestation, and oral contraceptive use were significantly associated with the presence of cervical dysplasia.

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