# Chapter 27 / Capítulo 27

*Screening, Diagnosis, and Prevention in Clinical Practice: Evidence from Argentine and Latin American Medicine (English Version)*
**ISBN:** 978-9915-704-33-3
**DOI:** 10.62486/978-9915-704-33-3.Ch27
**Pages:** 398-412

# Cyto-histological correlation in cervical cancer precursor lesions and evaluation of the Papanicolaou test as a screening method in samples analyzed at the Clinical Surgical Pathology Laboratory of the city of Rosario during the year 2024

## Correlación Cito-Histológica en lesiones precursoras de cáncer cérvico-uterino y evaluación del test de Papanicolaou como método de tamizaje en muestras analizadas en el Laboratorio de Patología Clínico Quirúrgica de la ciudad de Rosario durante el año 2024

Pablo Osuna[1], René German Laurito[1]

Universidad Abierta Interamericana, Facultad de Medicina y Ciencias de la Salud. Carrera de Medicina, Rosario. Argentina

**ABSTRACT**

**Introduction:** cervical-uterine cancer (CCU) represents one of the most common cancers in women, and its early detection is key to reduce its incidence and mortality. In Argentina, the high prevalence of precursor lesions and invasive carcinoma raises doubts about the efficacy of the Papanicolaou test (PAP) as a screening method. With a positive predictive value of approximately 60 %, PAP always requires confirmation by histologically directed biopsy. Therefore, this study analyzes the correlation between PAP cytological results and histological findings.
**Objective:** to correlate cytological findings obtained by PAP and histological results of cervical biopsies in samples analyzed at the Clinical Surgical Pathology Laboratory of the city of Rosario during the year 2024.
**Method:** quantitative, observational study, with a cross-sectional and retrospective correlational design. The population consisted of patients between 26 and 61 years old with positive PAP reports and later confirmed by histological biopsy.
**Results:** a total of 127 patients with positive Papanicolaou results (ASC-US, ASC-H, L-SIL and H-SIL) were analyzed. Of this group, only 27 patients (21,3 %) had a histological biopsy performed subsequently. The mean age was 40 ± 8,4 years (minimum 26 and maximum 61 years), with the most frequent age being 33 years. The predominant age group was.

**Keywords:** Cytohistological Correlation; Cervical Cancer; PAP; Squamous Intraepithelial Lesions; Cervical Cytology.

**RESUMEN**

**Introducción:** el cáncer cérvico-uterino (CCU) representa uno de los más comunes en las mujeres, y su detección temprana es clave para reducir su incidencia y mortalidad. En Argentina, la alta prevalencia de lesiones precursoras y carcinoma invasor genera dudas sobre la eficacia del test de Papanicolaou (PAP) como método de tamizaje. Con un valor predictivo positivo aproximado

del 60 %, el PAP requiere siempre confirmación mediante biopsia histológica dirigida. Por lo tanto este estudio analiza la correlación que existe entre los resultados citológicos del PAP y los hallazgos histológicos.
**Objetivo:** correlacionar los hallazgos citológicos obtenidos por PAP y los resultados histológicos de biopsias cervicales en muestras analizadas en el Laboratorio de Patología Clínico Quirúrgica de la ciudad de Rosario durante el año 2024.
**Método:** estudio cuantitativo, observacional, con un diseño correlacional de corte transversal y retrospectivo. La población estuvo conformada por pacientes de entre 26 y 61 años con informes de PAP positivos y que luego fueron confirmados por biopsia histológica.
**Results:** a total of 127 patients with positive Papanicolaou test results (ASC-US, ASC-H, L-SIL, and H-SIL) were analyzed. Of this group, only 27 patients (21,3 %) had a subsequent histological biopsy. The mean age was 40 ± 8,4 years (range 26–61 years), with the most frequent age being 33 years. The predominant age group was 39–48 years, representing 37 % of the total. In the concordance analysis between cytological and histological results, variations were observed according to the Papanicolaou test categories. 86 % of the ASC-US results corresponded to negative biopsies, while 78 % of the H-SIL results coincided with high-grade lesions on histology. In the case of L-SIL diagnoses, 57 % were confirmed as low-grade lesions, and 50 % of ASC-H cases were associated with H-SIL biopsies. Finally, when evaluating the effectiveness of the Papanicolaou test, 17 concordant cases (62,96 %) and 10 discordant cases (37,04 %) were identified.
**Conclusion:** the results of the study showed that the Papanicolaou test demonstrates good correlation with histological findings, particularly in the more severe categories such as H-SIL.

**Palabras clave:** Correlación Cito-Histológica; Cáncer Cérvico-Uterino; PAP; Lesiones Intraepiteliales Escamosas; Citología Cervical.

## INTRODUCTION

Cervical cancer (CC) continues to be one of the most common cancers among women worldwide, ranking fourth after breast, colorectal, and lung cancer. Annually, there are approximately 604,000 new cases worldwide, with an asymmetrical distribution, given that 85 % of cases occur in underdeveloped countries, where mortality from this cancer is high, reaching approximately 70 %, mainly due to late diagnosis (Sung et al., 2021).

In Argentina, around 4,500 new cases are diagnosed each year, representing the third most common cancer in women, and 2,500 women die from this disease. This is noteworthy, as in developed countries, the implementation of organized cytology-based programs has significantly reduced the incidence and mortality of CRC. This demonstrates that well-developed and implemented health policies can change the natural history of this disease (International Agency for Research on Cancer [IARC], 2020).

CCU has particular epidemiological characteristics, being more common in young women with limited access to healthcare and low socioeconomic and cultural status, who do not usually undergo regular check-ups or are not registered with the healthcare system for this purpose (Bruni et al., 2019; Sankaranarayanan et al., 2003).

It is also important to delve deeper into the natural history of human papillomavirus (HPV) infection and its link to CCU, given that 80 % of the general population comes into contact with the virus at some point in their lives. The interaction of HPV with the host's immune

system can lead to cancer precursor lesions in the lower genital tract (LGT), which, over time (approximately 10 to 20 years), can develop into invasive carcinoma. HPV infection is a necessary, but not sufficient, condition for the development of SCC (Bosch et al., 2002).

For more than 50 years, there has been growing interest in the early detection of HPV infection and its precursor lesions in order to interrupt its natural progression before the development of invasive carcinoma (Koss, 1989). The Papanicolaou (PAP) test, a cervical exfoliative cytology, has been a fundamental screening method, achieving a significant reduction in the incidence of CCU in countries with organized screening programs (Meggiolaro et al., 2016). However, in underdeveloped countries, screening is opportunistic, contributing to the high incidence of this disease (National Cancer Institute [NCIs], 2024).

Early detection of precursor lesions of cervical cancer is essential to reduce the incidence and mortality associated with this disease. Although PAP has been widely used globally as a screening tool, its effectiveness can vary considerably depending on the context, especially in resource-limited settings. A recent study conducted in Peru found that although the Pap test is commonly used, its sensitivity may not be sufficient to detect all high-grade intraepithelial lesions, potentially leading to late diagnoses and less effective treatments (Chacón-Byrne et al., 2024).

Another study conducted in African countries revealed that the detection rate of PAP varies significantly depending on factors such as health infrastructure and health education (Hailegebireal et al., 2024). According to this study, adapting screening programs to local characteristics could improve their effectiveness. In addition, it highlights the need to strengthen diagnostic capacity in regions where CCU mortality remains high due to late diagnosis and limited screening coverage.

The high prevalence of precursor lesions and invasive cervical carcinoma in Argentina raises questions about the actual effectiveness of the Pap test as a population screening method. Although the PAP has a positive predictive value (PPV) of approximately 60 %, it is considered a cytological test that only provides a diagnostic suspicion, which must be confirmed by a colposcopically guided histological biopsy (Meggiolaro et al., 2016; Toziano et al., 2022).

Several studies show that there is a significant and positive correlation between PAP cytological results and histological findings, making it an effective and reliable method for the diagnosis of precursor lesions of cervical cancer.

What is the correlation between cytological findings obtained by PAP and histological results of cervical biopsies in samples analyzed at the Clinical Surgical Pathology Laboratory in the city of Rosario during 2024?

*Objective*

To correlate cytological findings obtained by PAP and histological results of cervical biopsies in samples analyzed at the Clinical Surgical Pathology Laboratory in the city of Rosario during 2024.

## METHOD

### Design

The study was quantitative, observational, and used a cross-sectional, retrospective correlational design. The research lasted five months, from August to December 2024, while the collected data spanned from January 1 to December 31, 2024.

### Scope

The research was conducted at the Clinical Surgical Pathology Laboratory in Rosario, Santa Fe, Argentina. It is a private pathological anatomy laboratory located in the city center.

### Population and sample selection

The study population consisted of all women aged 18 to 70 who had not undergone a hysterectomy, from whom a Pap smear was obtained for evaluation and sent to the private Clinical Surgical Pathology Laboratory in Rosario. The following selection criteria were applied:

*Inclusion criteria*

- Patients with abnormal Pap smear results, followed by biopsy for further study of their case.

*Exclusion criteria*

- Patients with negative Pap smears and patients who have received prior treatment for HPV and/or pelvic cancer.

### Sampling and sample size

The research was conducted using non-probabilistic convenience sampling. The sample size consisted of those patients with abnormal Pap smear results, corroborated by histological biopsy during the study period.

### Procedures

The database of the Clinical Surgical Pathology Laboratory of Rosario was reviewed, which stored the results of Pap smears and histological biopsies.

Positive Pap smear results were then selected. These results were classified into four categories:

- Atypical squamous cells of undetermined significance (ASC-US)
- Atypical squamous cells where high-grade intraepithelial lesion cannot be excluded (ASC-H)
- Low-grade squamous intraepithelial lesions (LSIL)
- High-grade squamous intraepithelial lesions (HSIL)

The database was then searched to determine whether a subsequent histological biopsy was performed in those patients with a positive Pap test result. The results of these biopsies were classified as:

- LSIL
- HSIL
- Invasive carcinoma

Finally, the data obtained were recorded in an Excel spreadsheet, considering the study variables (patient age, Pap smear sample quality, Pap smear cytological result, and biopsy histological result).

*Definitions*

- Sample quality (representativeness of the Pap smear): The quality of the Pap smear samples obtained will be considered, classifying them as "representative" or "non-representative," depending on whether they meet the criteria established for proper interpretation of the test.
- Cytological result of the Pap test: result of the cervical cytology, categorizing the samples into different groups according to the Bethesda system. They will be recorded as "ASC-US; ASC-H; LSIL or HSIL."
- Histological result of the biopsy: result of the biopsy performed, categorizing the lesions as low-grade or high-grade "squamous intraepithelial lesion" (LSIL or HSIL) or "invasive carcinoma."

**Statistical analysis**

The data collected was entered into an Excel spreadsheet for further processing. Qualitative variables were analyzed using absolute and relative frequencies for each category. In contrast, quantitative variables were analyzed using measures of central tendency (mean, median) and measures of dispersion (range, standard deviation). The Chi-square test (X2) was used to assess the relationship between qualitative variables.

To study the effectiveness of the Pap test, the percentage of agreement and disagreement between cytological and histological findings was calculated.

For this purpose, cases in which a positive PAP (ASC-US, ASC-H, L-SIL, or H-SIL) was accompanied by a positive biopsy (L-SIL or H-SIL) were considered "agreements." Cases in which the PAP was positive but the biopsy was negative were considered "disagreements." (SIL or H-SIL). Cases in which the PAP was positive but the biopsy was negative were considered "discrepancies." The metrics were obtained by applying the following formulas:

Concordance (%) = (concordance / Case total)  100
Disconcordance (%) = (disconcordance / Case total)  100

**Ethical considerations**

The study was conducted in accordance with international and national ethical standards, including the Declaration of Helsinki and the Personal Data Protection Act (Law 25,326). The confidentiality and anonymity of patient data were guaranteed. The Medical School Administration endorsed the study.

## RESULTS

The population comprised of 127 patients with positive Pap smear results (ASC-US, ASC-H, L-SIL, and H-SIL). Of these, only 27 patients underwent histological biopsy after the positive result, representing 21,3 % of the total.

The average age of these patients was 40 ± 8,4 years. The minimum age recorded was 26 years, while the maximum was 61 years, indicating a range of 35 years. The most common age was 33 years, and the largest age group was patients aged 39 to 48 years, representing 37 % of the total, as shown in figure 2.

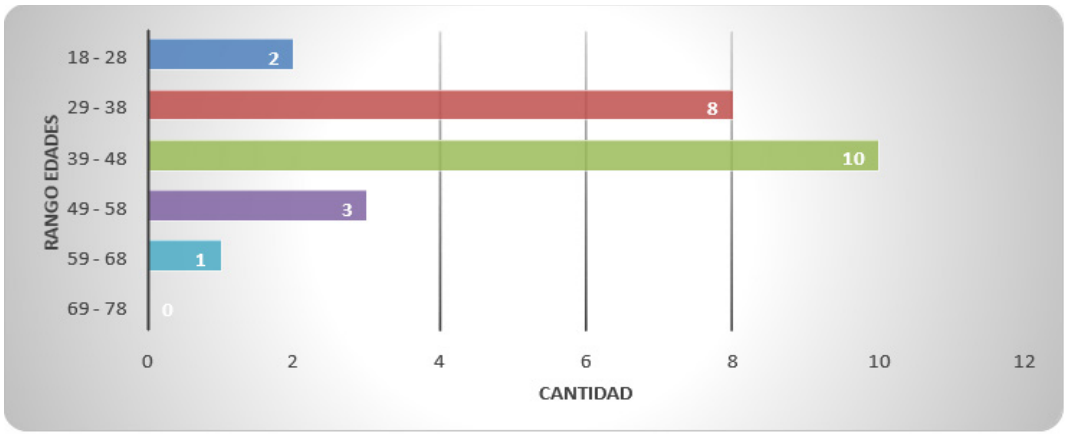


**Figure 1.** Distribution of patients according to age range

Table 1 shows the distribution of cytological diagnoses (ASC-US, ASC-H, L-SIL, H-SIL) and their correlation with histological diagnoses obtained by biopsy (negative, L-SIL, H-SIL).

**Table 1.** Distribution of cytological diagnoses and their correlation with histological diagnoses

| Pap/Biopsies | Negative | L-SIL | H-SIL | Total |
|---|---|---|---|---|
| ASC-US | 6 | 1 | 0 | 7 |
| ASC-H | 1 | 1 | 2 | 4 |
| L-SIL | 1 | 4 | 2 | 7 |
| H-SIL | 2 | 0 | 7 | 9 |
| Total | 10 | 6 | 11 | 27 |

The correlation between cytological findings and histological diagnoses showed some discrepancies. Eighty-six percent of ASC-US diagnoses corresponded to negative biopsies, while 50 % of ASC-H diagnoses were associated with H-SIL biopsies. In L-SIL samples, 57 % confirmed low-grade lesions in histology, while 78 % of H-SIL cytological diagnoses coincided with high-grade lesions in biopsies. This distribution is shown in figure 2.

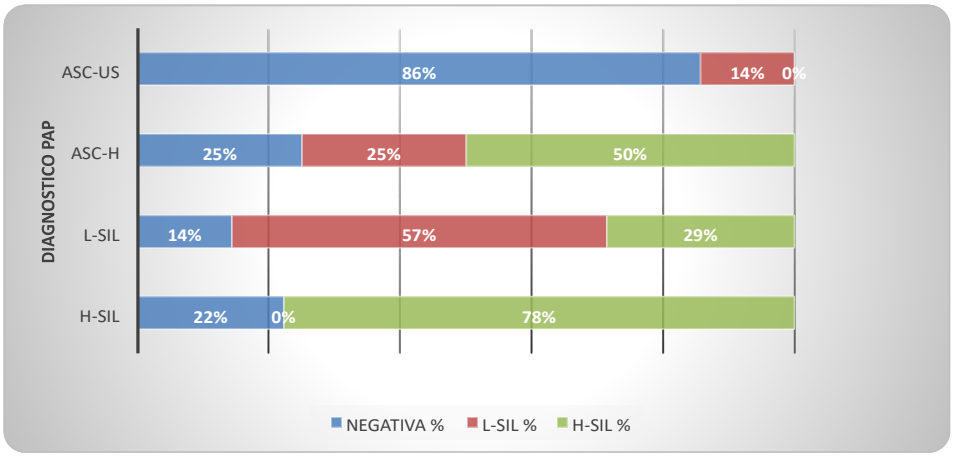


**Figure 2.** Correlation between cytological findings and histological diagnoses

Table 2 shows the distribution of histological diagnoses according to cytological findings from the Pap test.

**Table 2.** Distribution of histological diagnoses according to cytological findings from the Pap test

| Biopsies/PAP | ASC-US | ASC-H | L-SIL | H-SIL | Total |
|---|---|---|---|---|---|
| Negative | 6 | 1 | 1 | 2 | 10 |
| L-SIL | 1 | 1 | 4 | 0 | 6 |
| H-SIL | 0 | 2 | 2 | 7 | 11 |
| Total | 7 | 4 | 7 | 9 | 27 |

- Of the 10 cases with a negative histological diagnosis, 60 % corresponded to cytologies with ASC-US, followed by 20 % with H-SIL, 10 % with L-SIL, and 10 % with ASC-H.
- Among the 6 biopsies positive for L-SIL, the majority (66,7 %) presented L-SIL in the PAP, while the rest were divided equally (16,7 % each) between ASCUS and ASC-H.
- Finally, of the 11 biopsies diagnosed as H-SIL, 63,6 % corresponded to patients with H-SIL in the PAP, while 18,2 % had L-SIL, and another 18,2 % had ASC-H.

This is shown in figure 3:

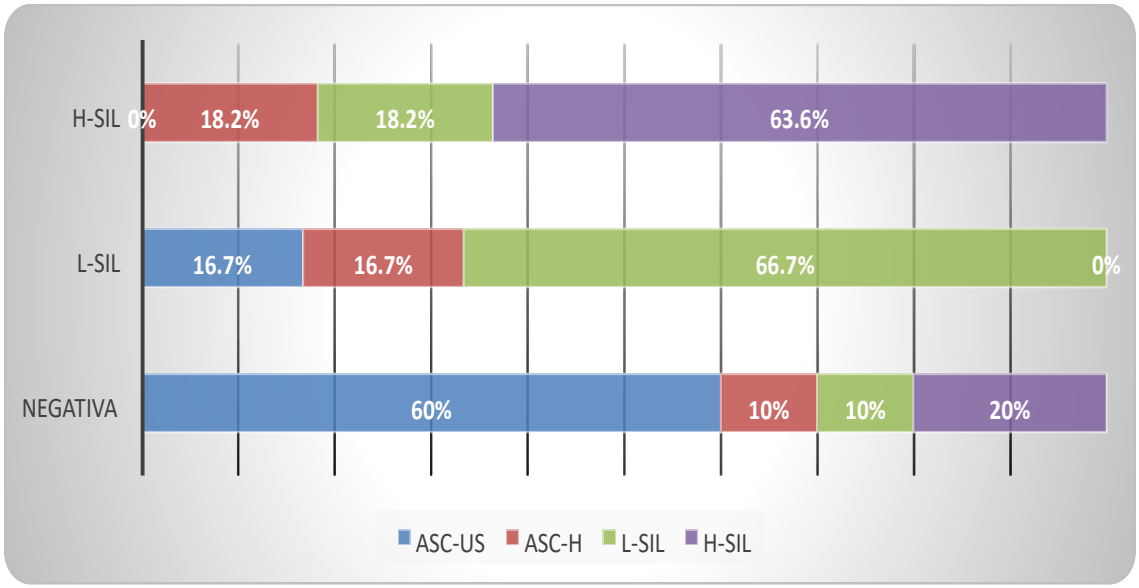


**Figure 3.** Distribution of patients according to histological biopsy results

To assess the effectiveness of the Pap test, the concordance and discordance rates between cytological and histological findings were calculated.

In this analysis, 17 concordant cases were identified, representing 62,96 % of the total, and 10 discordances, corresponding to 37,04 %, as shown in figure 4.

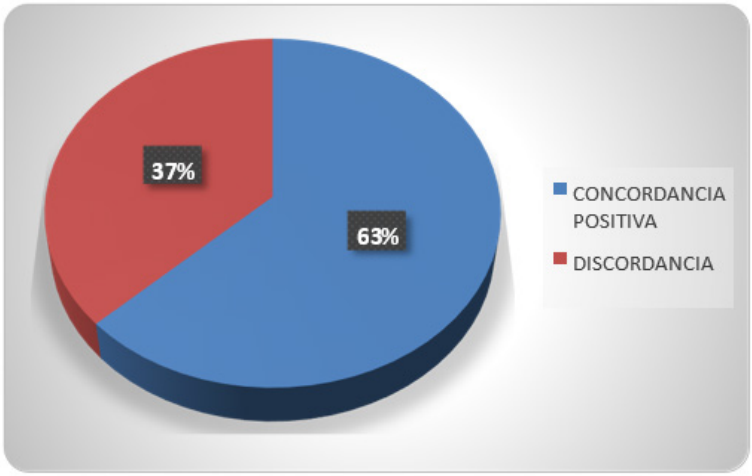


**Figure 4.** Effectiveness of the Pap test

## DISCUSSION

The results obtained in this study showed a significant correlation between cytological findings and histological diagnoses. In particular, 78 % of cases classified as H-SIL in cytology were confirmed as H-SIL in biopsy, demonstrating the high specificity of the Pap test for detecting high-grade lesions. This finding is consistent with previous studies indicating that the PAP test has high specificity for detecting high-grade lesions, especially in the presence of high-risk oncogenic HPV subtypes (Meggiolaro et al., 2016).

In contrast, only 57 % of cases classified as L-SIL on PAP testing were confirmed histologically, a figure within the range reported in previous studies (50 %–70 %). The spontaneous regression of a high proportion of L-SIL lesions, the low intrinsic evolutionary potential of this lesion type, and variability in both sample collection and histopathological evaluation can explain the lower concordance in these cases. In addition, in many centers, the usual approach to an L-SIL result is to perform periodic six-monthly cytology and colposcopy checks, which in many cases obviates the need for biopsies (Solomon et al., 2002).

On the other hand, 86 % of cases classified as ASC-US in cytology were negative on biopsy, confirming that this category has a low positive predictive value for high-grade lesions. Although only 14 % of these cases were HPV-associated, this percentage is not negligible and underscores the importance of surveillance and follow-up in patients with ASC-US. In this regard, it is recommended that PAP tests be repeated every 6 months or that high-risk HPV be detected by molecular testing to improve diagnostic accuracy (Nayar & Wilbur, 2015). In comparison, the ASC-H category showed a 50 % correlation with H-SIL on biopsy, suggesting that these cases are more likely to represent high-grade lesions and therefore require more rigorous colposcopic follow-up (Chacón-Byrne et al., 2024).

Overall, the global correlation between PAP and histology was 62,92 %, within the expected range for this screening method. However, these results highlight the limitations of the PAP as a single test and its low value when used in isolation as a population screening method. It is therefore essential to ensure systematic PAP sampling at appropriate intervals and optimized protocols to improve its diagnostic efficacy. Currently, the introduction of the HPV DNA test

aims to improve the sensitivity and specificity of screening for high-risk strains. This method is in the implementation phase and, when used in conjunction with the Pap test, is proposed for inclusion in a future systematic screening program.

Additionally, the false positive rate in this study was 37,04 %, a figure similar to that reported in previous studies. This percentage, together with the influence of factors such as inflammation, reactive metaplasia, sample quality, and errors in cytological interpretation, underscores the need for complementary diagnostic procedures. Colposcopy with targeted biopsy is therefore an essential strategy for confirming PAP findings and avoiding unnecessary interventions (Nayar & Wilbur, 2015).

The Pap test has proven to be instrumental in reducing the incidence and mortality of cervical cancer in countries that have implemented organized screening programs (IARC, 2020). However, in regions where screening is opportunistic, its impact is limited. There is a clear correlation between socioeconomic and cultural factors and the incidence/mortality of cervical cancer, especially in underdeveloped countries in Latin America, where cervical cancer is the second most common cancer in women. In Argentina, for example, mortality from this disease remains high, with significant disparities between geographic regions with less access to organized policies (e.g., Jujuy vs. Buenos Aires, with a mortality ratio of 5 to 1), indicating an urgent need to optimize screening coverage and quality (INC, 2024).

Previous studies have suggested that combining PAP with HPV testing could significantly improve diagnostic accuracy, especially in women over 30 years of age (Castle et al., 2012; Degenhardt et al., 2019). In this context, optimizing screening programs and implementing new strategies—such as self-sampling for HPV detection—could improve screening coverage and effectiveness in vulnerable populations (Hailegebireal et al., 2024). In addition, ongoing training of cytotechnologists and pathologists is crucial to minimize interobserver variability in cytological interpretation and, consequently, improve sample quality and diagnostic accuracy (Bosch et al., 2020).

In conclusion, the findings of this study support the usefulness of the Pap test as a screening tool for the early detection of precursor lesions of cervical cancer, while highlighting the need for complementary strategies to optimize its diagnostic effectiveness. The combination of cytology, HPV testing, and colposcopy appears to be the most promising approach to reduce the burden of this disease in the population, thereby improving early detection and timely intervention.

**Limitations**

As this is a single-center study, the results obtained cannot be extrapolated to all patients attending the various health centers in the city of Rosario.

The small sample size in the study limits the generalizability of the observations.

The fact that this is a retrospective study using secondary sources for data collection makes underreporting possible.

By working only with positive cytologies, the number of false negatives was unavailable, preventing the calculation of essential parameters such as the sensitivity and specificity of the Pap test.

Other factors that may influence the accuracy of the PAP, such as sample quality or laboratory processing conditions, were not considered, which could have affected the reliability of the cytological results.

## CONCLUSIONS

The correlation between positive cytological findings for HPV cervical lesions and their histological confirmation was determined to be 62,92 %. Comparison of diagnoses revealed that 78 % of H-SIL cases classified by cytology were confirmed by biopsy, whereas for LSIL cases, confirmation was 57 %. 14 % of ASC-US cases were positive for L-SIL on biopsy; in the ASC-H category, 50 % correlated with H-SIL on histology. A positive false rate of 37,04 % was observed.

## BIBLIOGRAPHIC REFERENCES

Agencia Internacional de Investigación sobre el Cáncer (IARC). (2020). *Cervical cancer* **(Global Cancer Observatory Fact Sheet).** https://gco.iarc.fr/today/data/factsheets/cancers/23-Cervix-uteri-fact-sheet.pdf

Arbyn, M., Weiderpass, E., Bruni, L., de Sanjosé, S., Saraiya, M., Ferlay, J., & Bray, F. (2020). Estimates of incidence and mortality of cervical cancer in 2018: A worldwide analysis. *The Lancet Global Health*, 8(2), e191-e203. https://doi.org/10.1016/S2214-109X(19)30482-6

Bishop, J. W., Heller, D. S., & Provenzano, D. A. (2019). *Diagnostic gynecologic and obstetric pathology* **(3rd ed.).** Elsevier.

Hailegebireal, A. H., Bizuayehu, H. M., & Tirore, L. L. (2024). Far behind 90-70-90's screening target: The prevalence and determinants of cervical cancer screening among Sub-Saharan African women: Evidence from Demographic and Health Survey. *BMC Cancer*, 24(1), Article 1140. https://doi.org/10.1186/s12885-024-12789-3

Bosch, F. X., Lorincz, A., Muñoz, N., Meijer, C. J. L. M., & Shah, K. V. (2002). The causal relation between human papillomavirus and cervical cancer. *Journal of Clinical Pathology*, 55(4), 244-265. https://doi.org/10.1136/jcp.55.4.244

Bosch, F. X., Broker, T. R., Forman, D., Moscicki, A. B., Gillison, M. L., Doorbar, J., & International HPV Study Group. (2013). Comprehensive control of human papillomavirus infections and related diseases. *Vaccine*, 31(7), H1-H31. https://doi.org/10.1016/j.vaccine.2013.10.003

Bruni, L., Albero, G., Serrano, B., Mena, M., Gómez, D., Muñoz, J., & Bosch, F. X. (2019). *Human papillomavirus and related diseases in the world: Summary report 17 June 2019*. ICO/IARC Information Centre on HPV and Cancer. https://hpvcentre.net/statistics/reports/XWX.pdf

Castle, P. E., Fetterman, B., Poitras, N. E., Lorey, T., Shaber, R., & Kinney, W. K. (2012). The natural history of human papillomavirus detection in cervical screening: A yearlong prospective study of HPV persistence. *Journal of Clinical Virology*, 54(4), 336-341. https://doi.org/10.1016/j.jcv.2012.04.018

Castellsagué, X., Díaz, M., de Sanjosé, S., Muñoz, N., Herrero, R., Franceschi, S., & International Agency for Research on Cancer Multicenter Cervical Cancer Study Group. (2018). Worldwide human papillomavirus etiology of cervical adenocarcinoma and its cofactors: Implications for screening and prevention. *Journal of the National Cancer Institute*, 98(5), 303-315. https://

doi.org/10.1093/jnci/djw208

Chacón-Byrne, S. R., Araujo-Banchon, W. J., & Gutarra-Vilchez, R. B. (2024). Capacidad diagnóstica de la colposcopía y citología en despistaje de lesiones de cuello uterino. *Revista del Cuerpo Médico Hospital Nacional Almanzor Aguinaga Asenjo*, 16(4). https://doi.org/10.35434/rcmhnaaa.2023.164.2129

Clifford, G., Franceschi, S., Diaz, M., Muñoz, N., & Villa, L. L. (2006). HPV type-distribution in women with and without cervical neoplastic diseases. *Vaccine*, 24(3), S26-S34. https://doi.org/10.1016/j.vaccine.2006.05.026

Cohen, P. A., Jhingran, A., Oaknin, A., & Denny, L. (2019). Cervical cancer. *The Lancet*, 393(10167), 169-182. https://doi.org/10.1016/S0140-6736(18)32470-X

Degenhardt, L., Wolfe, D., Hall, W., Hickman, M., Chang, J., Bruneau, J., & International Drug Policy Consortium. (2019). Strategies to reduce drug-related harm: Responding to the evidence base. *The Lancet*, 394(10208), 1490-1493. https://doi.org/10.1016/S0140-6736(19)32232-9

Doorbar, J., Quint, W., Banks, L., Bravo, I. G., Stoler, M., Broker, T. R., & Stanley, M. A. (2012). The biology and life-cycle of human papillomaviruses. *Vaccine*, 30(5), F55-F70. https://doi.org/10.1016/j.vaccine.2012.06.083

de Sanjosé, S., Brotons, M., & Pavón, M. A. (2017). The natural history of human papillomavirus infection. *Best Practice & Research Clinical Obstetrics & Gynaecology*, 47, 2-13. https://doi.org/10.1016/j.bpobgyn.2017.08.015

Holowaty, P., Miller, A. B., Rohan, T., & To, T. (1999). Natural history of dysplasia of the uterine cervix. *Journal of the National Cancer Institute*, 91(3), 252-258. https://doi.org/10.1093/jnci/91.3.252

Instituto Nacional del Cáncer (INC). (2024). *SIVER-Ca en base a los registros de mortalidad de la DEIS*. Ministerio de Salud de la Nación, Argentina. https://www.argentina.gob.ar/salud/instituto-nacional-del-cancer/institucional/siver-ca

Koss, L. G. (1989). The Papanicolaou test for cervical cancer detection: A triumph and a tragedy. *JAMA*, 261(5), 737-743. https://doi.org/10.1001/jama.1989.03420050089038

Massad, L. S., Einstein, M. H., Huh, W. K., Katki, H. A., Kinney, W. K., Schiffman, M., & Solomon, D. (2013). Long-term follow-up of women with cervical intraepithelial neoplasia: A study of outcomes and implications for management. *Obstetrics & Gynecology*, 121(6), 1389-1396. https://doi.org/10.1097/AOG.0b013e31829215b1

McIndoe, W. A., & Smith, J. E. (1984). The natural history of cervical intraepithelial neoplasia. *Obstetrics & Gynecology*, 63(6), 788-792.

Meggiolaro, A., Unim, B., Semyonov, L., Miccoli, S., Maffongelli, E., & La Torre, G. (2016). The role of Pap test screening against cervical cancer: A systematic review and meta-analysis. *La*

*Clinica Terapeutica*, 167(4), 124-139. https://doi.org/10.7417/CT.2016.1942

Melinkow, J., & Goodman, M. (1998). The natural history of cervical intraepithelial neoplasia: A review. *Journal of Women's Health*, 7(5), 609-616. https://doi.org/10.1089/jwh.1998.7.609

Miller, A. B., Sankaranarayanan, R., Bosch, F. X., & Sepúlveda, C. (2003). Can screening for cervical cancer be improved, especially in developing countries? *International Journal of Cancer*, 145(4), 884-893. https://doi.org/10.1002/ijc.11388

Mitchell, H., & Kehoe, S. T. (1994). Natural history of CIN: A study of 350 patients. *British Journal of Obstetrics and Gynaecology*, 101(11), 1094-1097. https://doi.org/10.1111/j.1471-0528.1994.tb13718.x

Muñoz, N., Bosch, F. X., de Sanjosé, S., Herrero, R., Castellsagué, X., Shah, K. V., & International Agency for Research on Cancer Multicenter Cervical Cancer Study Group. (2003). Epidemiologic classification of human papillomavirus types associated with cervical cancer. *New England Journal of Medicine*, 348(6), 518-527. https://doi.org/10.1056/NEJMoa021641

Nanda, K., Satcher, L., & Eltoum, I. (2000). Accuracy of the Papanicolaou test in screening for and follow-up of cervical cytologic abnormalities: A systematic review. *Obstetrics & Gynecology*, 95(4), 625-634. https://doi.org/10.1016/S0029-7844(00)00975-0

Nayar, R., & Wilbur, D. C. (2015). *The Bethesda System for Reporting Cervical Cytology: Definitions, criteria, and explanatory notes*. Springer. https://doi.org/10.1007/978-3-319-11074-5

Ostor, A. G. J., & Cummings, R. (1993). Natural history of cervical intraepithelial neoplasia: A review. *Journal of Clinical Pathology*, 46(10), 885-887. https://doi.org/10.1136/jcp.46.10.885

Prendiville, W., Cullimore, J., & Norman, S. (1989). Large loop excision of the transformation zone (LLETZ): A new method of management for women with cervical intraepithelial neoplasia. *BJOG: An International Journal of Obstetrics & Gynaecology*, 96(9), 1054-1060. https://doi.org/10.1111/j.1471-0528.1989.tb03241.x

Plummer, M., Herrero, R., Franceschi, S., Meijer, C. J., Snijders, P., Bosch, F. X., & International Agency for Research on Cancer Multicenter Cervical Cancer Study Group. (2003). Smoking and cervical cancer: Pooled analysis of the IARC multi-centric case–control study. *Cancer Causes & Control*, 14(9), 805-814. https://doi.org/10.1023/B:CACO.0000003867.66025.20

Ronco, G., Dillner, J., Franceschi, S., & Minshew, J. (2014). HPV vaccination and cervical cancer screening. *The Lancet Oncology*, 15(10), e461-e468. https://doi.org/10.1016/S1470-2045(14)70283-4

Richart, R. M. (1968). Cervical intraepithelial neoplasia. *Obstetrics & Gynecology*, 31(3), 390-394. https://doi.org/10.1097/00006250-196803000-00016

Sankaranarayanan, R., Nene, B. M., Dinshaw, K., Rajkumar, R., Shastri, S., Wesley, R., & IARC Multicentre Study Group. (2003). Early detection of cervical cancer with visual

inspection methods: A summary of completed and ongoing studies in India. *Salud Pública de México*, 45(Suppl. 3), S399-S407. https://www.scielo.org.mx/pdf/spm/v45s3/v45s3a14.pdf

Sasieni, P., Castanon, A., & Cuzick, J. (2009). Effectiveness of cervical screening with age: Population based case-control study of prospectively recorded data. *BMJ*, 339, b2968. https://doi.org/10.1136/bmj.b2968

Saslow, D., Solomon, D., Lawson, H. W., Killackey, M., Kulasingam, S. L., Cain, J., & American Cancer Society. (2012). American Cancer Society guidelines for the early detection of cervical cancer. *CA: A Cancer Journal for Clinicians*, 62(3), 147-172. https://doi.org/10.3322/caac.21039

Sherman, M. E., Lorincz, A. T., Scott, D. R., Wacholder, S., Castle, P. E., Glass, A. G., & Schiffman, M. (2003). Baseline cytology, human papillomavirus testing, and risk for cervical neoplasia: A 10-year cohort analysis. *Journal of the National Cancer Institute*, 95(1), 46-52. https://doi.org/10.1093/jnci/95.1.46

Solomon, D., Davey, D., Kurman, R., Moriarty, A., O'Connor, D., Prey, M., & Stoler, M. (2002). The 2001 Bethesda System: Terminology for reporting results of cervical cytology. *JAMA*, 287(16), 2114-2119. https://doi.org/10.1001/jama.287.16.2114

Sung, H., Ferlay, J., Siegel, R. L., Laversanne, M., Soerjomataram, I., Jemal, A., & Bray, F. (2021). Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: A Cancer Journal for Clinicians*, 71(3), 209-249. https://doi.org/10.3322/caac.21660

Tomita, L. Y., Longatto-Filho, A., Costa, M. C., Andreoli, M. A., Villa, L. L., Franco, E. L., & Cardoso, M. A. (2010). Dietary patterns and risk of cervical intraepithelial neoplasia. *Nutrition and Cancer*, 62(7), 849-857. https://doi.org/10.1080/01635581.2010.509834

Toziano, M., Gogorza, S., & Daguerre, P. (Eds.). (2022). *Prevención primaria y secundaria del cáncer cervicouterino: manejo del tamizaje anormal y de las lesiones histológicas del cuello uterino*. SAPTGIyC – SOGIBA. (Aval Académico de FASGO)

Trottier, H., & Franco, E. L. (2006). The epidemiology of genital human papillomavirus infection. *Vaccine*, 24(Suppl. 1), S1-S15. https://doi.org/10.1016/j.vaccine.2005.09.054

Vaccarella, S., Lortet-Tieulent, J., Plummer, M., Franceschi, S., & Bray, F. (2013). Worldwide trends in cervical cancer incidence: Impact of screening against changes in disease risk factors. *European Journal of Cancer*, 49(15), 3262-3273. https://doi.org/10.1016/j.ejca.2013.04.024

Wright, T. C., Jr., Cox, J. T., Massad, L. S., Twiggs, L. B., & Wilkinson, E. J. (2001). 2001 Consensus Guidelines for the management of women with cervical cytological abnormalities. *Journal of Lower Genital Tract Disease*, 5(3), 183-203. https://doi.org/10.1097/00128360-200107000-00001

World Health Organization. (2020). *Global strategy to accelerate the elimination of cervical cancer*

*as a public health problem*. https://www.who.int/publications/i/item/9789240014107