



## EDITORIAL

# PRECURSOR LESIONS OF ANAL CANCER IN WOMEN: APPROACH FROM THE GYNECOLOGIST'S PERSPECTIVE

**H**uman papilloma virus (HPV) infection is the most frequent sexually transmitted infection worldwide. In 2010, it was estimated that in women with normal cytology, the global prevalence of HPV infection ranged between 7 and 11%, while the prevalence in Latin America and the Caribbean was 6%, one of the highest in the world (1). HPV is the second infectious cause of cancer after bacterial infection by *Helicobacter pylori* (2). In the United States, nearly 45,300 new HPV-associated cancer cases were estimated between 2013 and 2017, especially of anogenital and oropharyngeal cancer (3).

HPV-associated cancer risk found for cervical and anal cancer are 100% and 88% respectively (4). Squamous-cell anal carcinoma is caused mainly by serotypes 16 and 18, considered of high oncogenic risk (4), based on the finding of HPV DNA, mainly of subtypes 16 (80%) and 18 (10%) (5), in anal biopsies of squamous-cell neoplasms performed in European, Asian and North-American populations. Anal cancer accounts for nearly 1-2% of gastrointestinal cancers and it is estimated that, in the United States, close to 4,700 new cases of HPV-associated anal cancer occur in women and 2,300 in men every year (2). In Colombia, age-adjusted incidence for the period 2010-2012 ranged between 0.5 and 1.9 x 100,000 women per year, and from 0.5 to 0.9 for every 100,000 men per year (6). Regarding mortality due to anal cancer, it is estimated that close to 1,350 people will have died due to this cancer in 2020 (7).

Women with a history of cervical intraepithelial neoplasia (CIN) have been described to be at a higher risk of anal infection by high oncogenic risk HPV than those with no history of CIN (17.4 vs 1.5% respectively); moreover, this virus has been found to infect both the cervical and the anal mucosa in 4% of women with CIN (8). There is also evidence that women with a history of grade 3 CIN are at a higher risk of developing anal cancer, with an incidence rate ratio (IRR) of 3.85 (95% CI: 2.32-6.37), and of developing grade 3 anal intraepithelial neoplasia (IRR: 6.68; 95% CI: 3.64-12.25) (9).

Within this context, anal intraepithelial neoplasia (AIN) is part of a multicomponent disease of the lower genital tract; therefore, the presence of cervical, vaginal and vulvar intraepithelial neoplasia may trigger an alert on the presence or future emergence of anal intraepithelial lesions (10). In Colombia, few studies have examined the prevalence of anal intraepithelial neoplasia in women with lower genital tract dysplasia. In 2018, Gomez *et al.* published a study of 119 women with a histopathological diagnosis of CIN2/3 and carcinoma *in situ*, reporting a 6.7% prevalence of AIN (7 women with low grade AIN and one case of high grade AIN). Anal HPV infection was found in 45 women (37.8%), with HPV 16 and 18 being the predominant genotypes (11).

There is a stark contrast between this landscape of higher risk of anal cancer, particularly in women with a history of CIN, and the little interest found

among gynecologist regarding this perineal and perianal pathology. This issue of RCOG features an exploratory study of the prevalence of high-risk HPV infection in the anal mucosa of women with a recent diagnosis of CIN in the city of Bogota. This study is important because it seeks to create awareness among government agencies, insurance companies, obstetricians and gynecologists, and researchers of the risk of AIN in women with a history of lower genital tract dysplasia of any grade.

For government agencies, it is relevant to determine whether the implementation of guidelines for the prevention and early diagnosis of high-risk anal HPV infection and of AIN in women at a high risk for anal cancer (history for CIN and HIV infection) is effective and safe (12). For specialists in obstetrics and gynecology, it is relevant to warn female patients about this possibility and to recognize the need to expand the scope of the annual gynecological exam to include the routine assessment of the perianal area; moreover, specialists should also become aware of the usefulness of alternative screening for AIN. It is worth remembering that the most widely used tests for AIN screening and diagnosis, as reported in the literature, are anal cytology - reported with the Bethesda system - together with digital anorectal exam (DARE) (12) and high resolution anoscopy (13). Also, units working with lower genital tract and colposcopy pathology should consider the creation of multidisciplinary teams for the diagnosis and care of women with premalignant conditions, including AIN.

Finally, researchers working with lower genital tract pathology should conduct studies in high risk populations to determine the frequency of anal infection due to HPV 16 and 18, and to assess screening tests for accuracy and also for their effectiveness safety and acceptability in our setting. Likewise, the role of vaccination against high-risk HPV in preventing this disease condition should also be assessed (14).

It is worth remembering that many women trust their ob/gyn doctor as their primary care practitioner

from whom they expect guidance as well as intervention or early detection of any morbid conditions that may affect them.

### **Jorge Andrés Rubio-Romero**

Associate Editor

Revista Colombiana de Obstetricia y Ginecología (RCOG)

### **Luz Amparo Díaz-Cruz**

Associate Professor

Obstetrics and Gynecology Department,  
Universidad Nacional de Colombia

## **REFERENCES**

1. Bruni L, Diaz M, Castellsagué X, Ferrer E, Bosch FX, de Sanjosé S. Cervical human papillomavirus prevalence in 5 continents: Meta-analysis of 1 million women with normal cytological findings. *J Infect Dis.* 2010;202(12):1789-99. <https://doi.org/10.1086/657321>
2. de Martel C, Georges D, Bray F, Ferlay J, Clifford GM. Global burden of cancer attributable to infections in 2018: A worldwide incidence analysis. *Lancet Glob Health.* 2020;8(2):e180-e190. [https://doi.org/10.1016/S2214-109X\(19\)30488-7](https://doi.org/10.1016/S2214-109X(19)30488-7)
3. Centers for Disease Control and Prevention. Cancers associated with human papillomavirus, United States—2013-2017. *United States Cancer Statistics Data Brief.* 2020;18. Available in: <https://www.cdc.gov/cancer/uscs/pdf/USCS-DataBrief-No18-September2020-h.pdf>
4. de Martel C, Plummer M, Vignat J, Franceschi S. Worldwide burden of cancer attributable to HPV by site, country and HPV type. *Int J Cancer.* 2017;141(4):664-70. <https://doi.org/10.1002/ijc.30716>
5. Alemany L, Saunier M, Alvarado-Cabrero I, Quirós B, Salmeron J, Shin HR, et al. Human papillomavirus DNA prevalence and type distribution in anal carcinomas worldwide. *Int J Cancer.* 2015;136(1):98-107. <https://doi.org/10.1002/ijc.28963>

6. Bruni L, Albero G, Serrano B, Mena M, Gómez D, Muñoz J, et al. Human papillomavirus and related diseases in the world - Summary report. ICO/IARC Inf Cent HPV Cancer (HPV Inf Centre). 2019;307. Available in: <https://hpvcentre.net/statistics/reports/XWX.pdf>
7. National Cancer Institute. Surveillance, epidemiology and end results program. Cancer Stat Facts: Anal Cancer. 2018. Available in: <https://seer.cancer.gov/statfacts/html/anus.html>
8. Bregar AJ, Cronin B, Luis C, DiSilvestro P, Schechter S, Pisharodi L, et al. Anal and cervical high-risk human papillomavirus genotyping in women with and without genital neoplasia. *J Low Genit Tract Dis.* 2018;22(2):115-9. <https://doi.org/10.1097/LGT.0000000000000368>
9. Ebisch RMF, Rutten DWE, Int'Hout J, Melchers WJG, Massuger LFAG, Bulten J, et al. Long-lasting increased risk of human papillomavirus-related carcinomas and premalignancies after cervical intraepithelial neoplasia grade 3: A population-based cohort study. *J Clin Oncol.* 2017;35(22):2542-50. <https://doi.org/10.1200/JCO.2016.71.4543>
10. Tatti S, Suzuki V, Fleider L, Maldonado V, Caruso R, Timirello M de L. Anal intraepithelial lesions in women with human papillomavirus-related disease. *J Low Genit Tract Dis.* 2012;16(4):454-9. <https://doi.org/10.1097/LGT.0b013e31825d2d7a>
11. Gómez S, Castillo M, Amaya J, Restrepo O, Puentes E y Sanabria D. Prevalencia de neoplasia intraepitelial, infección por VPH y alteraciones en citología anal en mujeres con LEI de alto grado y cáncer in situ de cérvix en una población de Bogotá. Trabajos ganadores presentados en el XXXI Congreso Nacional de Obstetricia y Ginecología realizado del 9 al 12 de mayo de 2018 en Cartagena, Colombia. *Rev Colomb Obstet Ginecol.* 2018;69(3):218-21. Available in: <https://revista.fecolsog.org/index.php/rcog/article/view/3234>
12. Alam NN, White DA, Narang SK, Daniels IR, Smart NJ. Systematic review of guidelines for the assessment and management of high-grade anal intraepithelial neoplasia (AIN II/III). *Colorectal Dis.* 2016;18(2):135-46. <https://doi.org/10.1111/codi.13215>
13. Bull-Henry K, Morris B, Buchwald UK. The importance of anal cancer screening and high-resolution anoscopy to gastroenterology practice. *Curr Opin Gastroenterol.* 2020;36(5):393-401. <https://doi.org/10.1097/MOG.0000000000000661>
14. Roden RBS, Stern PL. Opportunities and challenges for human papillomavirus vaccination in cancer. *Nat Rev Cancer.* 2018;18(4):240-54. <https://doi.org/10.1038/nrc.2018.13>