Original Article

Histopathological Spectrum of Cervical Lesions in Relation to HPV Status: A Cross-Sectional Study from a Tertiary Care Centre

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Abstract

Background: Cervical cancer remains a leading cause of morbidity and mortality among women worldwide, with human papillomavirus (HPV) recognized as its primary etiological agent. Histopathological examination remains the cornerstone of diagnosis, while HPV testing provides critical etiological and prognostic insights. **Material and Methods:** A cross-sectional observational study was conducted in the Department of Pathology, SRM Medical College, from January 2022 to December 2023. A total of 150 patients with clinically suspected cervical lesions were included. Biopsy and hysterectomy specimens were processed using routine histopathology and classified according to the WHO 2020 guidelines. HPV DNA detection and genotyping were performed using PCR-based methods. Data were analyzed using SPSS v25.0, and associations were tested with the Chi-square method. **Results:** The majority of patients were in the 41–50-year age group (33.3%), with abnormal vaginal bleeding as the most common symptom (46.7%). Histopathology revealed squamous cell carcinoma (30%) as the predominant lesion, followed by chronic cervicitis (26.7%), LSIL (20%), HSIL (16.7%), and adenocarcinoma (6.7%). Overall, 95 cases (63.3%) were HPV-positive, with HPV 16 (52.6%) and HPV 18 (26.3%) as the most frequent genotypes. HPV positivity was significantly associated with lesion severity, being highest in HSIL (88.0%) and squamous cell carcinoma (88.9%) ($p < 0.05$). **Conclusion:** This study reinforces the strong association between high-risk HPV, particularly types 16 and 18, and cervical neoplasia. Integrating histopathology with HPV testing enhances diagnostic accuracy, aids risk stratification, and strengthens prevention strategies. The findings further highlight the public health importance of HPV vaccination in reducing cervical cancer burden.

Keywords: Cervical lesions, Histopathology, HPV, Squamous cell carcinoma, HSIL, HPV genotyping.

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Introduction

Cervical cancer is a major health issue for women around the world, especially in developing countries. The World Health Organization reports that it is the fourth most common cancer in women, with an estimated 604,000 new cases and 342,000 deaths in 2020.[1] Cervical lesions, which can be benign, precancerous, or malignant, are key early signs of this disease. Identifying and treating these lesions early is vital for reducing illness and death. A persistent infection with high-risk Human Papillomavirus (HPV), particularly types 16 and 18, is the main cause of cervical intraepithelial neoplasia and cervical cancer.[2] The viral oncogenes E6 and E7 promote cancer by disabling tumor suppressor proteins like p53 and Rb, leading to uncontrolled cell growth.[3] In this situation, histopathological examination is the best method for accurately diagnosing cervical lesions. It provides information on the tissues' structure and helps with grading and staging, which are important for effective clinical management.[4]

The Bethesda System for cytology and the World Health Organization's histopathological criteria have facilitated streamlined classification of cervical lesions. The latter are commonly categorized as low-grade squamous intraepithelial lesions (LSIL), high-grade lesions (HSIL), and invasive carcinomas.[5] While there is cogent evidence regarding the oncogenic role of HPV itself, its precise correlation with HPV positivity and range of histopathology is ever-changing. There is evidence to indicate that high-risk types of HPV are strongly associated with high-grade lesions and invasive squamous cell carcinoma and are less frequently seen in benign/mildly abnormal lesions and normal cervix and vaginae.[6] Low-risk types are seen more frequently in benign/mildly abnormal lesions and normal cervix and vaginae. However, divergences concerning the predominance of genotype and the histopathology pattern among different people have been observed. Despite increased vaccination about HPV and cytology-based screening, there is an imperative need for comprehensive data from those tertiary care units, which are referral and sentinel sites, and represent all possible cases. They can provide informative data regarding regional disease patterns

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and support prevention activities.[7]

This present investigation endeavours to determine the scope of cervical lesion histopathology and to study its association with HPV status among patients who present at a referral care centre. Specifically, it would like to determine the rate of positivity to HPV among different histology classes, study the association of the status for HPV with lesion severity, and ascertain the association with clinical variables such as age and presentation. The findings can inform improved techniques for screening, detection of high-risk patients to follow up, and inclusion of testing for HPV as a routine diagnostic procedure. This can ultimately facilitate early detection, prevention, and reduction of the overall burden from cervical cancer.

Materials and Methods

Study design and setting: This cross-sectional observational study was conducted in the Department of Pathology, SRM Medical College], a tertiary care referral centre catering to urban and rural populations. It was carried out over two years, from January 2022 to December 2023. The Institutional Ethics Committee approved the study, and informed written consent was obtained from all participants prior to inclusion.[8]

Patient selection and sampling: A total of 150 patients presenting with clinically suspected cervical lesions and undergoing biopsy or hysterectomy were included. Inclusion criteria comprised: (i) patients with cervical biopsies showing adequate tissue, (ii) cases ranging from benign lesions to premalignant and malignant changes, and (iii) availability of sufficient material for HPV testing. Exclusion criteria included recurrent cervical malignancies, cases with inadequate or autolyzed specimens, and patients unwilling to participate. A consecutive sampling technique was adopted, including all eligible cases during the study period. Demographic data such as age, parity, and presenting complaints (e.g., abnormal vaginal bleeding, discharge, post-coital bleeding) were recorded in a structured proforma.[9]

Histopathological examination: Biopsy and hysterectomy specimens were immediately fixed in 10% neutral buffered formalin for at least 12–24 hours. Standard tissue processing was performed, followed by paraffin embedding. Sections of 4–5 µm thickness were cut and stained with Hematoxylin and Eosin (H&E).[10] Special stains and immunohistochemistry (p16, Ki-67) were applied in selected cases to confirm dysplastic or malignant lesions.[11] Lesions were classified according to the WHO 2020 classification of female genital tract tumors into.[12]

- Benign lesions (chronic cervicitis, squamous metaplasia, endocervical polyps)
- Premalignant lesions (LSIL, HSIL)
- Malignant lesions (squamous cell carcinoma, adenocarcinoma, adenosquamous carcinoma, and others).

HPV testing: HPV detection was carried out on formalin-fixed paraffin-embedded (FFPE) tissue samples. DNA was extracted using the Qiagen QIAamp DNA Mini Kit following the manufacturer's instructions. Polymerase chain reaction (PCR) was employed using consensus primers (MY09/MY11 and GP5+/GP6+) targeting the L1 region of the HPV genome.[13] Positive samples underwent genotyping for high-risk HPV (types 16, 18, 31, 33, 45) and low-risk HPV (types 6, 11) using type-specific primers.[14] Internal controls were included in each run, and 10% of samples were randomly retested to ensure reproducibility. Cases were categorized as HPV-positive or HPV-negative based on PCR results.[15]

Data analysis: Data were tabulated using Microsoft Excel 2019 and analyzed with SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize patient demographics, histopathological categories, and HPV positivity rates. The Chi-square test was applied to assess associations between HPV status and different histopathological groups. Odds ratios with 95% confidence intervals were calculated where appropriate. A p-value < 0.05 was considered statistically significant.[16]

Results

A total of 150 patients with cervical lesions were studied. The age distribution of participants is shown in Table 1. Most cases occurred in the 41–50 age group (33.3%), followed by 31–40 years (26.7%). Only 10% of cases were above 60 years. The age distribution curve [Figure 1] demonstrates a peak incidence in the perimenopausal group.

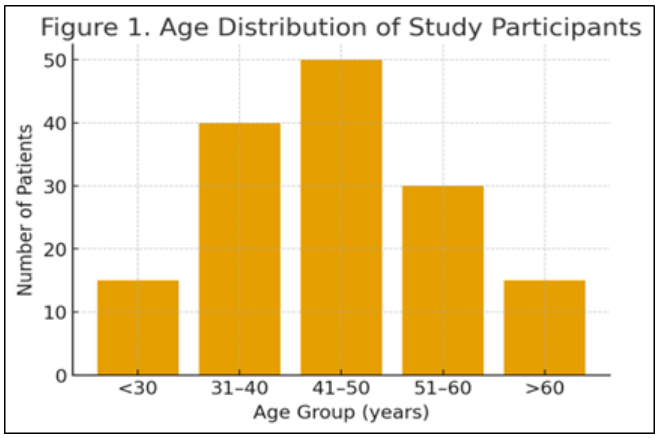


Table 1: Age Distribution of Study Participants (n = 150)

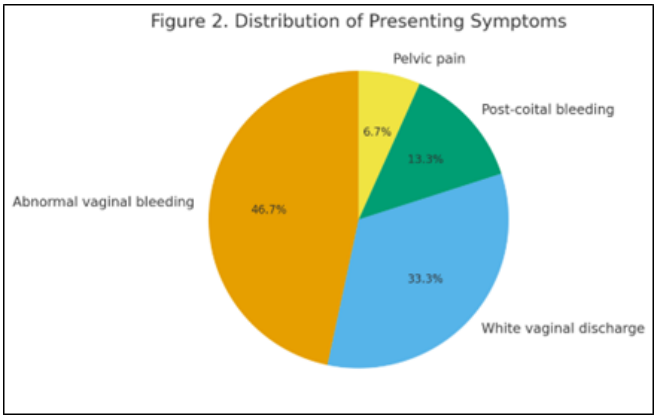
Age Group (years)	Number of Patients	Percentage (%)
<30	15	10.0
31–40	40	26.7
41–50	50	33.3
51–60	30	20.0
>60	15	10.0

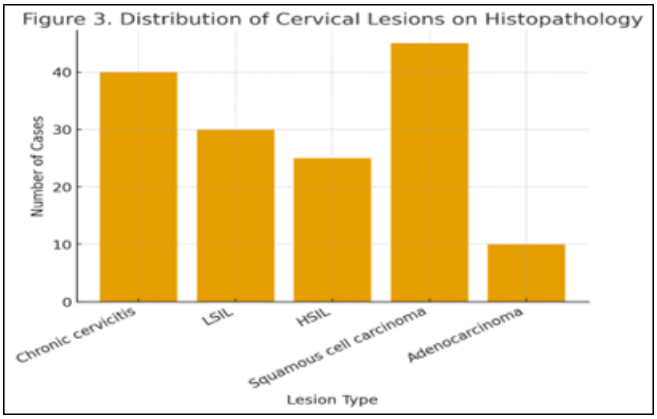
With respect to clinical history, abnormal vaginal bleeding was the most common symptom, present in 70 patients

(46.7%), followed by white vaginal discharge in 50 cases (33.3%), post-coital bleeding in 20 cases (13.3%), and pelvic pain in 10 cases (6.7%). The presenting complaint distribution is summarized in Table 2 and depicted in [Figure 2].

Table 2: Presenting Symptoms of Patients (n = 150)

Symptom	Number of Patients	Percentage (%)
Abnormal vaginal bleeding	70	46.7
White vaginal discharge	50	33.3
Post-coital bleeding	20	13.3
Pelvic pain	10	6.7





Histopathological examination revealed a wide spectrum of cervical lesions. Squamous cell carcinoma was the most frequent diagnosis, seen in 45 cases (30%), followed by chronic cervicitis in 40 cases (26.7%), LSIL in 30 cases (20%), HSIL in 25 cases (16.7%), and adenocarcinoma in 10 cases (6.7%). The overall histopathological distribution is detailed in [Table 3] and illustrated in [Figure 3]. Rare variants such as basaloid and adenosquamous carcinoma were observed in isolated cases.

HPV DNA testing showed that 95 patients (63.3%) were HPV positive, while 55 (36.7%) were negative (Table 4, Figure 4). Among the HPV-positive cases, HPV 16 was the predominant genotype, detected in 52.6%, followed by HPV 18 in 26.3%, while other high-risk types such as HPV 31, 33, and 45 accounted for smaller proportions. Low-risk HPV types (6/11) were identified in only three cases (3.2%). The distribution of HPV genotypes is presented in [Table 5 and Figure 5].

Table 3: Histopathological Spectrum of Cervical Lesions (n = 150)

Diagnosis	Number of Cases	Percentage (%)
Chronic cervicitis	40	26.7
LSIL	30	20.0
HSIL	25	16.7
Squamous cell carcinoma	45	30.0
Adenocarcinoma	10	6.7

Table 4: Overall HPV Status (n = 150)

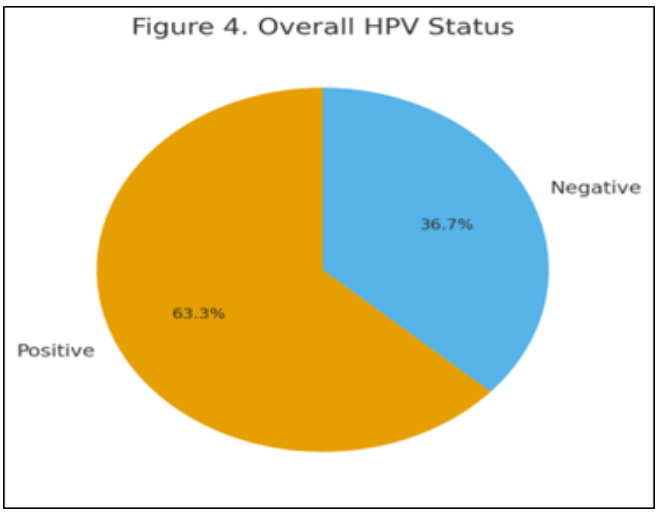
HPV Status	Number of Cases	Percentage (%)
Positive	95	63.3
Negative	55	36.7

Table 5: Distribution of HPV Genotypes among Positive Cases (n = 95)

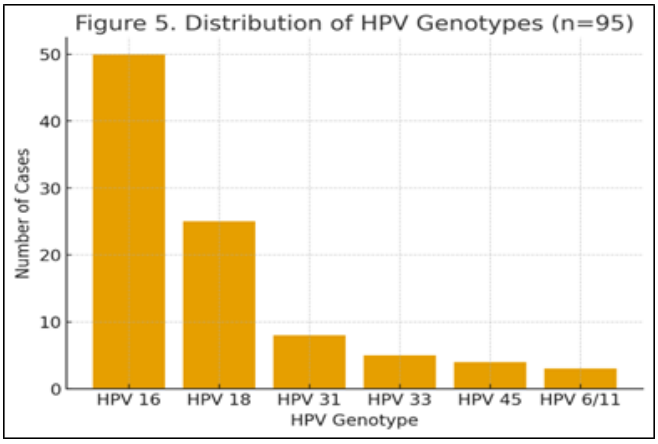
HPV Genotype	Number of Cases	Percentage (%)
HPV 16	50	52.6
HPV 18	25	26.3
HPV 31	8	8.4
HPV 33	5	5.3
HPV 45	4	4.2
HPV 6/11	3	3.2

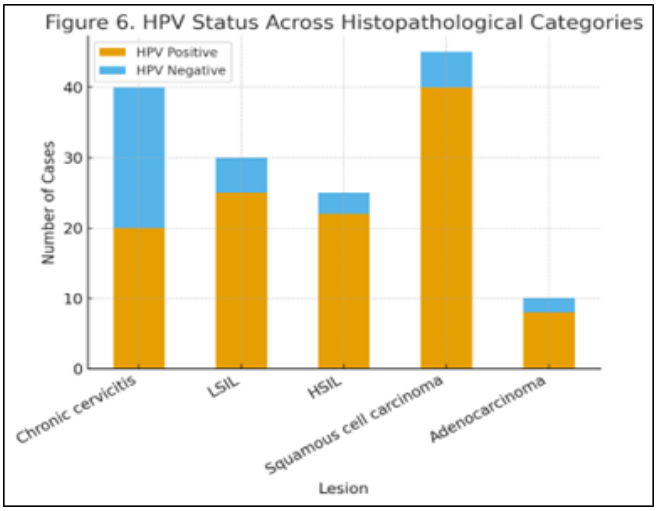
Table 6: Correlation between Histopathology and HPV Status (n = 150)

Lesion Type	Total Cases	HPV Positive (n)	HPV Negative (n)	HPV Positivity (%)
Chronic cervicitis	40	20	20	50.0
LSIL	30	25	5	83.3
HSIL	25	22	3	88.0
Squamous cell carcinoma	45	40	5	88.9
Adenocarcinoma	10	8	2	80.0



When correlating histopathological categories with HPV status [Table 6, Figure 6], HPV positivity was highest in squamous cell carcinoma (88.9%) and HSIL (88.0%), followed closely by LSIL (83.3%). In contrast, only 50% of chronic cervicitis cases were HPV positive. Among adenocarcinomas, 80% were associated with HPV infection. Statistical analysis using the Chi-square test showed a significant association between HPV status and lesion severity ($p < 0.05$).





Incidental findings included one case each of adenosquamous carcinoma and basaloid squamous cell carcinoma, both of which tested positive for high-risk HPV types (HPV 18 and HPV 16, respectively). No unusual distribution of low-risk HPV types was observed.

Discussion

This study explored the spectrum of histopathological cervical lesions and their correlation with HPV status at a referral care center. We found squamous cell carcinoma to be the most frequent malignant lesion at 30 percent, and HSIL and LSIL to account for most premalignant ones. Importantly, we found HPV DNA to be present in 63.3 percent of all cases studied, and high-risk type 16 and 18 to account for nearly 80 percent of all infections. We found a statistically significant correlation to exist between lesion severity and positivity for HPV, with positivity being highest among HSIL and invasive carcinomas.

Our observations are comparable with those from prior work conducted in India and other regions, and confirm 16 and 18 to be responsible for the majority of high-grade lesions and invasive cancers.[17,18] The high presence of HPV among samples of precancerous lesions in this population conforms to the known oncogenic contribution by HPV to cervical carcinoma.[19] The comparatively reduced detection rate among benign lesions like chronic cervicitis (50%) is likely a marker for transient infection(s) or simultaneous non-HPV pathologies. Similar findings have been reported by other histopathology-based studies.[20]

The intimate relationship of high-risk HPV and advanced lesions thus highlights the value of combining HPV testing with cervical cancer screening initiatives. The latter remain vital but are complemented by an added degree of sensibility by HPV testing for recognition of high-grade precancerous lesions.[21] At a management level, HPV-positive HSIL and carcinoma can demand tighter follow-up and more aggressive therapeutic measures compared to their respective HPV-negative counterparts.

Moreover, the predominance of HPV 16 and 18 in this population reinforces the importance of prophylactic HPV vaccine, directed at these genotypes and already demonstrating substantial reduction in disease burden from HPV where it has been introduced.[22,23] The information validates value added through effective vaccination policy in middle- and low-income countries, where cervical cancer is a leading cause of death.

The strength of this study is its coverage of all imaginable lesion kinds. It combines histopathology and molecular detection of HPV to obtain a complete range of lesion coverage regarding viral causality. The detection of benign and malignant lesions provides superior coverage of cervical pathology in a referral case scenario.

However, there are certain limitations to consider: Firstly, it is a one-centre trial with a relatively small sample size (n=150), and therefore it is likely to fail to account for genotype heterogeneity at a national or regional level. Secondly, the cross-sectional design precludes investigating change from low- to high-grade lesions over time. Thirdly, it is purely based upon PCR-based detection, but it may fail to differentiate transient from persistent infection.[24] The variables sexual history, smoking, and HIV

status, individually known to influence HPVV persistence, were not explored exhaustively.

Future studies would be advantaged by enrolling larger, multicenter populations to provide wider genotype distribution data for different regions. Longitudinal follow-up inclusion would allow examination of lesion progression and HPV infection duration with informative data about natural history. Diagnostic specificity for HPV-related lesions can further be enhanced by inclusion of p16 and Ki-67 immunohistochemistry in larger data sets.[25] The molecular definition of less common HPVs would similarly merit high priority in enhancing information about their clinical significance.[26]

Conclusion

This study demonstrates that squamous cell carcinoma is the most common cervical malignancy, and that HPV, particularly types 16 and 18, is strongly associated with high-grade lesions and invasive cancers. The significant correlation between HPV status and lesion severity underscores HPV's central role in cervical carcinogenesis.

Our findings support the integration of histopathology and HPV testing in cervical cancer screening and management. Such an approach enhances diagnostic accuracy and reinforces the importance of HPV vaccination programs in reducing disease burden.[27,28]

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. World Health Organization. Cervical cancer [Internet]. 2022 [cited 2025 Sep 19]. Available from: https://www.who.int/news-room/fact-sheets/detail/cervical-cancer
2. Bosch FX, de Sanjosé S. Human papillomavirus and cervical cancer—burden and assessment of causality. J Natl Cancer Inst Monogr. 2003;(31):3–13.
3. Moody CA, Laimins LA. Human papillomavirus oncoproteins: pathways to transformation. Nat Rev Cancer. 2010 Aug;10(8):550–60.
4. Bhatla N, Aoki D, Sharma DN, Sankaranarayanan R. Cancer of the cervix uteri. Int J Gynaecol Obstet. 2018 Oct;143 Suppl 2:22–36.
5. Solomon D, Nayar R. The Bethesda System for reporting cervical cytology: definitions, criteria, and explanatory notes. 3rd ed. New York: Springer; 2015.
6. Clifford GM, Smith JS, Plummer M, Muñoz N, Franceschi S. Human papillomavirus types in invasive cervical cancer worldwide: a meta-analysis. Br J Cancer. 2003 Jan;88(1):63–73.
7. Arbyn M, Weiderpass E, Bruni L, de Sanjosé S, Saraiya M, Ferlay J, et al. Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis. Lancet Glob Health. 2020 Feb;8(2):e191–203.
8. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013;310(20):2191–4.
9. Nayar R, Wilbur DC. The Pap test and Bethesda 2014: "the reports of my demise have been greatly exaggerated". J Low Genit Tract Dis. 2015;19(3):175–84.
10. Bancroft JD, Gamble M. Theory and practice of histological techniques. 7th ed. London: Churchill Livingstone; 2013.
11. Klaes R, Friedrich T, Spitkovsky D, et al. Overexpression of p16(INK4a) as a specific marker for the cervix uteri's dysplastic and neoplastic epithelial cells. Int J Cancer. 2001;92(2):276–84.
12. WHO Classification of Tumours Editorial Board. Female Genital Tumours. 5th ed. Lyon: IARC; 2020.
13. Manos MM, Ting Y, Wright DK, Lewis AJ, Broker TR, Wolinsky SM. Use of polymerase chain reaction amplification for the detection of genital human papillomaviruses. Cancer Cells. 1989;7:209 14.
14. Bernard HU, Chan SY, Manos MM, et al. Identifying and assessing known and novel human papillomaviruses by polymerase chain reaction amplification, restriction fragment length polymorphisms, nucleotide sequence, and phylogenetic algorithms. J Infect Dis. 1994;170(5):1077–85.
15. Clifford GM, Franceschi S. HPV in cervical cancer screening and vaccination. Vaccine. 2008;26 Suppl 10:K1–13.
16. Kirkpatrick LA, Feeney BC. A simple guide to IBM SPSS Statistics for version 25.0. Belmont, CA: Wadsworth; 2019.
17. Singh P, Gupta N, Nijhawan R, Srinivasan R. Spectrum of cervical lesions in North India: a hospital-based study. Indian J Pathol Microbiol. 2018;61(2):234–9.
18. Arbyn M, Castellsagué X, de Sanjosé S, et al. Worldwide burden of cervical cancer in 2008. Ann Oncol. 2011;22(12):2675–86.
19. Walboomers JM, Jacobs MV, Manos MM, et al. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. J Pathol. 1999;189(1):12–9.
20. Cuschieri K, Whitley MJ, Cubie HA, et al. HPV type-specific DNA and p16 expression in cervical intraepithelial neoplasia. J Clin Pathol. 2004;57(7):684–7.
21. Sankaranarayanan R, Nene BM, Shastri SS, et al. HPV screening for cervical cancer in rural India. N Engl J Med. 2009;360(14):1385–94.
22. Bosch FX, Lorincz A, Muñoz N, Meijer CJ, Shah KV. The causal relation between human papillomavirus and cervical cancer. J Clin Pathol. 2002;55(4):244–65.
23. Drolet M, Bénard É, Pérez N, et al. Population-level impact and herd effects following the introduction of human papillomavirus vaccination programmes: updated systematic review and meta-analysis. Lancet. 2019;394(10197):497–509.
24. Clifford GM, Franceschi S. HPV in cervical cancer screening and vaccination. Vaccine. 2008;26 Suppl 10:K1–13.
25. Klaes R, Friedrich T, Spitkovsky D, et al. Overexpression of p16(INK4a) as a specific marker for the cervix uteri's dysplastic and neoplastic epithelial cells. Int J Cancer. 2001;92(2):276–84.
26. Alemany L, Saunier M, Tinoco L, et al. Large-scale study of HPV DNA prevalence in cervical cancer: new insights into the role of less common HPV genotypes. Int J Cancer. 2014;135(11):2598–606.
27. Arbyn M, Weiderpass E, Bruni L, et al. Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis. Lancet Glob Health. 2020;8(2):e191–203.
28. Bruni L, Saura-Lázaro A, Montoliu A, et al. HPV vaccination introduction worldwide and WHO and UNICEF estimates of national HPV immunization coverage 2010–2019. Prev Med. 2021;144:106399.