

<https://doi.org/10.54500/2790-1203-2025-5-125-amj001>

Morphological Characteristics of Cervical Intraepithelial Neoplasia in the Context of Human Papillomavirus Infection-Associated Pathology

[Bakytaly Ibraimov](#) ^{1*}, [Talshyn Ukybasova](#) ², [Mahabbat Galym](#) ³, [Sanimkul Makhambetova](#) ⁴, [Dana Baktybayeva](#) ⁵,
[Kuralay Konrtay](#) ⁶, [Nazira Kamzayeva](#) ⁷, [Aizhan Toktarkhan](#) ⁸, [Aidana Nurgazykyzy](#) ⁹

¹ Head of the Pathological Anatomy Unit of the Clinical and Academic Department of Laboratory medicine, Pathology and genetics, Corporate Fund «University Medical Center», Astana, Kazakhstan

² Gynecologist, Clinical Academic Department of Women's Health, Corporate Fund «University Medical Center», Astana, Kazakhstan

Received: 20.04.2025

Accepted: 25.06.2025

Published: 31.10.2025

³ Obstetrician-gynecologist, highest qualification category, Clinical Academic Department of Women's Health, Corporate Fund «University Medical Center», Astana, Kazakhstan

* Corresponding author:

Bakytaly Ibraimov,

E-mail:

Bakytali.Ibrayimov@umc.org.kz

⁴ Obstetrician-gynecologist, Clinical Academic Department of Women's Health, Corporate Fund «University Medical Center», Astana, Kazakhstan

⁵ Gynecologist, Clinical and Academic Department of Women's Health, Corporate Fund «University Medical Center», Astana, Kazakhstan

Citation: Astana Medical Journal, 2025, 125 (5), amj001.

This work is licensed under a Creative

Commons Attribution 4.0 International

License

⁶ Gynecologist, Clinical Academic Department of Women's Health, Corporate Fund «University Medical Center», Astana, Kazakhstan

⁷ Gynecologist, Clinical Academic Department of Women's Health, Corporate Fund «University Medical Center», Astana, Kazakhstan

⁸ Pathologist, Clinical and Academic Department of Laboratory Medicine, Pathology and Genetics, Corporate Fund «University Medical Center», Astana, Kazakhstan

⁹ Pathologist, Clinical and Academic Department of Laboratory Medicine, Pathology and Genetics, Corporate Fund «University Medical Center», Astana, Kazakhstan



Abstract

Objective. To systematize the morphological characteristics of cervical intraepithelial neoplasia (CIN) in the context of human papillomavirus infection (HPV)-associated pathology through a literature review and analysis of clinical and morphological data.

Materials and Methods. The study included 40 cervical biopsy specimens obtained from patients with precancerous cervical conditions examined at the Department of Pathological Anatomy, University Medical Center. Histological evaluation was

performed using hematoxylin–eosin staining. Clinical and laboratory data were integrated, including Pap smear results, HPV genotyping, and screening for sexually transmitted infections (STIs).

Results. HPV type 16 was the most frequently detected genotype (14 cases). Coinfections with two HPV genotypes were observed in 9 patients (e.g., 16 and 45, 18 and 51), while 3 patients had triple infections. Sixteen cases were HPV-negative. High-grade CIN (CIN 2, CIN 3, or carcinoma in situ) was diagnosed in 19 of 40 patients (47.5%), even though cytology revealed only low-grade lesions (LSIL) or atypical squamous cells of undetermined significance (ASC-US). Additionally, 4 cases (10%) with NILM (negative for intraepithelial lesion or malignancy) on cytology demonstrated CIN I–II on histology. STIs were identified in 26 patients (65%), predominantly *Gardnerella vaginalis* (55%), followed by Cytomegalovirus (17.5%), *Candida albicans* (10%), and *Mycoplasma hominis* (7.5%), including mixed infections. These findings indicate a high prevalence of HPV and concurrent STIs among patients with CIN, as well as notable discrepancies between cytological and histological diagnoses, particularly in the presence of inflammatory processes.

Conclusions. The study underscores the limitations of cytological screening and the importance of comprehensive diagnostic strategies combining morphological, clinical, and molecular methods. Standardization of morphological criteria for CIN is essential, particularly in HPV-associated and inflammation-related contexts, to improve diagnostic accuracy and patient management.

Keywords: cervical intraepithelial neoplasia, HPV, cytology-histology correlation, sexually transmitted infections, morphology.

1. Introduction

Cervical cancer (CC) is the fourth most frequently diagnosed cancer and the fourth leading cause of mortality in women [1]. According to WHO estimates, in 2022 more than 660,000 new cases and approximately 350,000 deaths were registered globally, with over 90% of deaths occurring in low- and middle-income countries [2]. The incidence is mainly concentrated among women aged 25–59 years, with a peak risk between 45 and 49 years [1]. In Europe, approximately 66,000 new cases of cervical cancer and more than 30,000 deaths are recorded each year, according to the European Cancer Registry [3]. In Kazakhstan, CC incidence remains stable at approximately 19 per 100,000 women, while mortality rates have declined from 7.15 to 5.93 per 100,000, with

significant disparities in screening participation between urban (74%) and rural (38%) populations [4].

Cervical intraepithelial neoplasia (CIN) develops through infection by high-risk human papillomavirus (HPV) types, predominantly HPV 16 and 18, which penetrate the basal epithelial layer and establish persistent infection [5,6]. Viral genome integration disrupts oncogene expression, particularly E6 and E7 proteins. E6 induces p53 degradation, reducing apoptosis and DNA repair capacity, while E7 inactivates retinoblastoma protein (pRb), disrupting cell cycle control [7,8]. Viral integration often disrupts the E2 gene, which normally suppresses E6 and E7 expression, enhancing oncogenic effect [9]. These changes lead to genetic abnormalities, chromosomal instability, and

mutations, reflected in the pathomorphological spectrum from mild dysplasia (CIN I) to severe dysplasia (CIN III), characterized by disorganized epithelial stratification, nuclear atypia, and increased mitotic activity [10–12].

In 2020, the WHO published a new classification introducing a two-tier system: low-grade squamous intraepithelial lesions (LSIL/CIN I) and high-grade squamous intraepithelial lesions (HSIL), encompassing CIN II and CIN III [13]. However, the three-tier CIN classification remains widely used in practice. LSIL (CIN I) is characterized by abnormal changes limited to the lower third of epithelium with atypical proliferation, mitoses confined to basal layers, koilocytotic atypia, and preserved cytoplasmic maturation. HSIL (CIN II) demonstrates basal/parabasal morphology with mitotic activity extending to the lower two-thirds, while HSIL (CIN III) displays atypia throughout full epithelial thickness with immature cells and lack of superficial differentiation [14,15].

According to WHO, 99% of HSIL and invasive cervical cancer are caused by HPV and can be detected early with organized screening programs [1]. Recommended detection methods include HPV testing, cervical cytology, and colposcopy; however, microscopic histopathological assessment remains the diagnostic gold standard [14]. Despite modern screening protocols, CIN diagnosis relies heavily on morphological interpretation.

A comprehensive approach combining histological verification with virological and cytological data provides more accurate patient risk stratification and helps to avoid both under- and overtreatment.

However, interpretation presents challenges due to inter-observer variability, especially in borderline cases such as CIN I/II or CIN I/III [16]. Background inflammatory changes may mimic or obscure dysplastic processes, complicating differential diagnosis. Moreover, cytological screening frequently underestimates lesion severity compared to histology, leading to delayed diagnosis and treatment. Given the high prevalence of HPV infection among women of reproductive age, particularly in developing countries where vaccination rates are low and screening irregular, early detection of precancerous lesions remains a pressing global health issue. These challenges underscore the critical importance of standardizing CIN diagnostics and integrating morphological and molecular approaches into healthcare systems [17].

Aim of the Study - to identify and analyze discrepancies between morphological, cytological, and PCR data in the diagnosis of HPV-associated cervical pathology, based on 40 clinical cases examined at the Department of Pathological Anatomy, «University Medical Center» (Astana, Kazakhstan).

2. Materials and methods

This study represents a prospective analysis of pathomorphological and clinical-laboratory characteristics of 40 patients diagnosed with CIN between February and June 2025. The study included women aged 18–45 years referred to the “Center for the Prevention and Treatment of Precancerous Cervical Diseases,” established at CF “UMC” as part of a state-targeted funding program of the Ministry of Science and Education of the Republic of Kazakhstan. Patients were selected following HPV testing and Pap smear examination. Histopathological studies were conducted at the Department of Pathological Anatomy, CF “UMC,”

Astana (Kazakhstan), between February and June 2025. Histological materials were obtained from 40 women aged 18–45 years who underwent morphological verification of cervical intraepithelial neoplasia.

The objects of study were cervical biopsy specimens collected during diagnostic evaluation. Lesions were classified in accordance with the most recent WHO recommendations [13]. Based on morphological analysis, cases were distributed as follows: CIN I – 11 cases, CIN II – 18 cases, CIN III – 9 cases (including 4 cases of carcinoma in situ).

Histological processing was carried out using a standard protocol: fixation in 10% neutral formalin, passage through graded alcohols, paraffin embedding, sectioning at 3–5 µm thickness with a microtome, followed by hematoxylin–eosin (H&E) staining. Morphological evaluation was performed under a light microscope at magnifications ×100, ×200, and ×400, with analysis of epithelial architecture, degree of nuclear atypia, mitotic activity, and architectural abnormalities. All cases were classified according to the accepted CIN grading system (CIN I–III, CIS).

Microscopic diagnosis of koilocytosis in histological specimens is considered insufficiently

reliable due to subjective interpretation and possible morphological overlap with other epithelial alterations. Therefore, in this study, assessment of HPV-related changes relied primarily on cytological analysis.

This study was approved by the Local Bioethics Committee of the UMC Corporate Foundation (protocol #2024/02-013, 10/05/2024), and all patients provided informed consent for the use of their medical data in research. Morphological findings were correlated with clinical data, and when available, with cytological results and HPV status.

3. Results and discussion

The study included 40 patients with a confirmed diagnosis of CIN. The age of the patients ranged from 20 to 46 years, with a mean age of 31.5 ± 6.3 years and a median of 31 years. Most patients (72.5%) were within the

25–39 age group, corresponding to the peak reproductive period and emphasizing the importance of timely screening in this cohort (Table 1).

Table 1 – Age distribution of patients

Number of cases	Age distribution of patients
0	16-19 years
3	20-24 years
9	25-29 years
10	30-34 years
10	35-39 years

The distribution of CIN grades was as follows: CIN I – 11 cases, CIN II – 18 cases, CIN III – 9 cases (including carcinoma in situ). Two cases were not confirmed histologically and were diagnosed as chronic cervicitis.

Histopathological assessment confirmed the presence of hallmark features of cervical intraepithelial dysplasia in all cases, including nuclear enlargement, hyperchromasia, and increased mitotic activity, with the severity of these changes correlating with CIN grade.

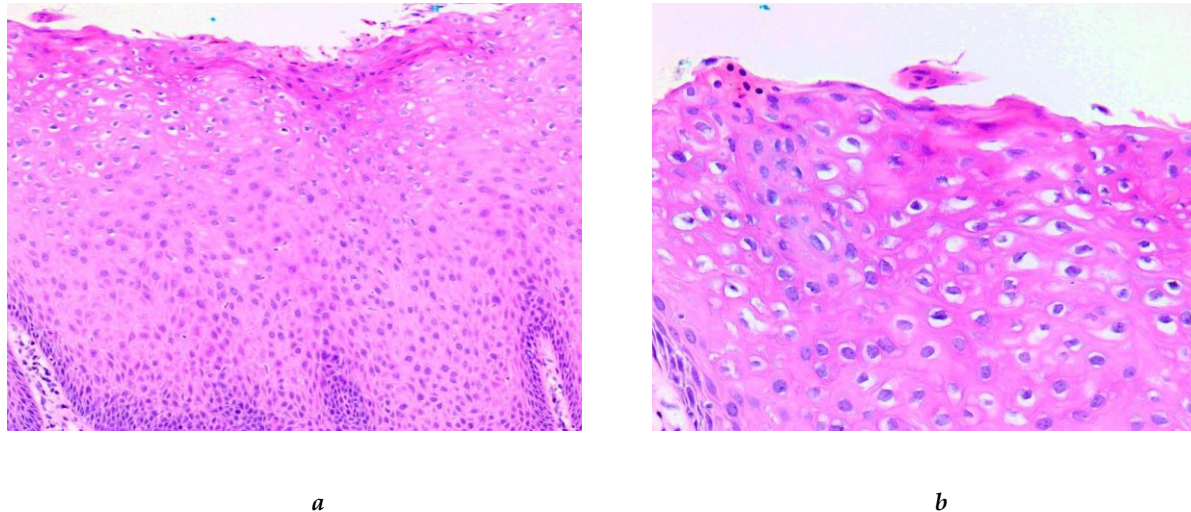


Figure 1- Histopathological features of LSIL (CIN I) (a) area of stratified squamous epithelium with features of CIN I: cells with moderate nuclear atypia, preserved differentiation, and koilocytosis in the superficial layers. (b) LSIL showing hyperchromatic nuclei with irregular membranes, variability in cell shape and size, and distinct perinuclear halos in the superficial layers.

Staining: Hematoxylin–eosin, magnification: a × 100, b × 400

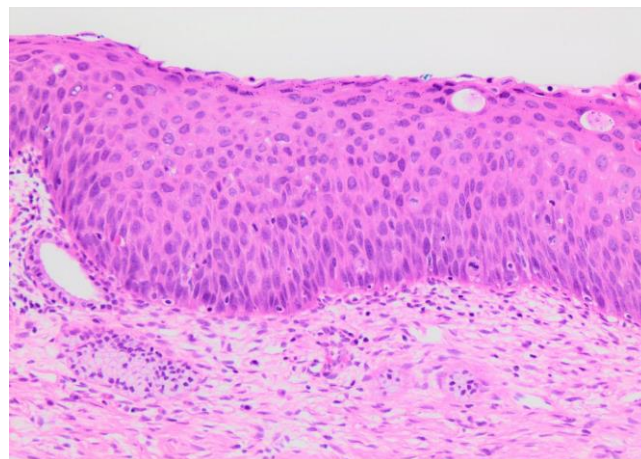


Figure 2— Histopathological features of HSIL (CIN II). Staining: Hematoxylin–eosin, magnification: × 200

At higher magnification, the epithelium demonstrates diffuse nuclear enlargement, with nuclei appearing significantly increased in size. These enlarged nuclei exhibit hyperchromasia, appearing intensely dark-stained, and exhibit irregular nuclear contours with abnormal shapes deviating from normal smooth outlines. Cytoplasmic differentiation is preserved in the upper

third of the epithelium. This combination of lower-layer nuclear atypia with retained superficial differentiation is consistent with HSIL/CIN II. Increased mitotic activity is observed in the lower and middle epithelial thirds, showing enhanced cell division in these regions. These features collectively support the diagnosis of HSIL/CIN II.

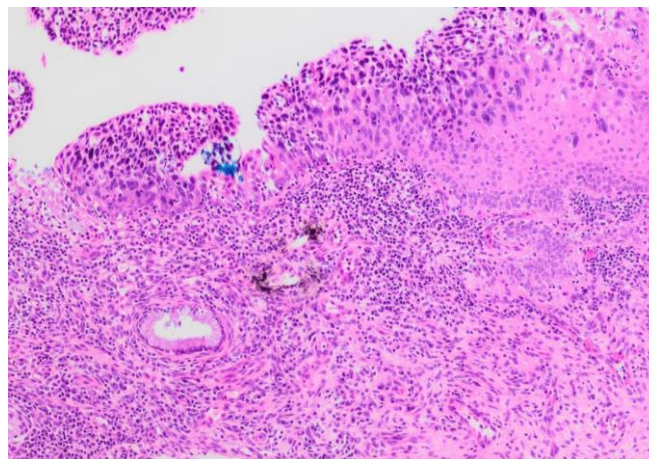


Figure 3 - Histopathological features of HSIL (CIN III). Staining: Hematoxylin-eosin, magnification: × 100

Representative photomicrographs showing histological features of HSIL/CIN III demonstrate focal pronounced nuclear pleomorphism with nuclei showing marked variation in size, shape, and staining intensity. Multinucleated cells are present, displaying multiple enlarged, irregular nuclei within single cell boundaries.

These features indicate severe dysplastic changes with loss of normal cellular uniformity. The nuclear pleomorphism and presence of multinucleated cells represent advanced cytopathic effects characteristic of high-grade intraepithelial neoplasia, consistent with CIN III classification.

Table 2 - Histopathological assessment

Patient, №	Histology	Pap smear results	HPV typing	Sexually transmitted infections (STIs)
1	Nabothian cysts of the cervix, chronic cervicitis	ASC-US	39	
2	CIN I, cervicitis	LSIL	16	
3	CIN I, cervicitis	LSIL		Gardnerella vaginalis Cytomegalovirus Candida albicans
4	CIN III, chronic cervicitis	LSIL	16	Gardnerella vaginalis Cytomegalovirus Mycoplasma hominis
5	CIN II	ASC-US		Gardnerella vaginalis Ureaplasma urealyticum
6	CIN II, cervicitis	LSIL		
7	CIN II, cervicitis	LSIL	52	Cytomegalovirus
9	CIN I, cervicitis	NILM		Gardnerella vaginalis
10	CIN II, cervicitis	ASC-US		
11	CIN III	LSIL	16	Gardnerella vaginalis
12	CIN I	LSIL	33	

13	CIN I, cervicitis	ASC-US		Gardnerella vaginalis
14	Squamous cell carcinoma in situ of the cervix with involvement of endocervical crypts. Cervicitis	ASC-H (HSIL)	52,58	Gardnerella vaginalis Cytomegalovirus Candida albicans
16	CIN III	ASC-H (HSIL)	16	
17	CIN II, cervicitis	NILM	31,58	Gardnerella vaginalis
18	CIN I	LSIL	39	Gardnerella vaginalis
19	CIN II, cervicitis	LSIL		Gardnerella vaginalis
20	CIN II, cervicitis	ASC-H (HSIL)	16,45	Gardnerella vaginalis
21	CIN I, cervicitis	ASC-US	52	
22	CIN II, cervicitis, Nabothian cysts of the cervix	LSIL		Gardnerella vaginalis Cytomegalovirus
23	Carcinoma in situ of the cervix with foci of microinvasion	ASC-H (HSIL)	16,45,58	Gardnerella vaginalis
24	Glandular ectopy of the cervical columnar epithelium with areas of squamous metaplasia. Dysplasia of the surface epithelium, grade II	ASC-H (HSIL)	16,35	Cytomegalovirus
25	CIN III, carcinoma in situ, cervicitis	ASC-US	16	Gardnerella vaginalis Cytomegalovirus Candida albicans
26	CIN II, cervicitis	ASC-US	16,59	
27	Carcinoma in situ, cervicitis	LSIL	16,18,45	Mycoplasma hominis
28	CIN II	LSIL		
29	CIN III, nabothian cysts of the cervix	ASC-US		Gardnerella vaginalis
30	CIN II	NILM	51	Gardnerella vaginalis Mycoplasma hominis
31	CIN III	LSIL	16	Gardnerella vaginalis
32	CIN II, cervicitis	LSIL	16/45	Chlamydia trachomatis
33	CIN II, cervicitis	NILM		Gardnerella vaginalis
34	CIN I	LSIL	18,51	
35	CIN II, cervicitis	ASC-US		
36	CIN II, cervicitis	LSIL	16,39	Gardnerella vaginalis
37	CIN I	LSIL	16,51	Gardnerella vaginalis
38	CIN I, cervicitis	ASC-H (HSIL)	33,52,58	Gardnerella vaginalis
39	CIN I	LSIL	33,56	Gardnerella vaginalis Candida albicans Ureaplasma urealyticum
40	CIN II	LSIL	59	
41	Chronic cervicitis	ASC-US	-	
42	CIN II	LSIL	33	

* CIN - Cervical Intraepithelial Neoplasia

ASC-US - Atypical Squamous Cells of Undetermined Significance

LSIL - Low-grade squamous intraepithelial lesion

ASC-H (HSIL) - Atypical Squamous Cells, High-grade Squamous Intraepithelial Lesion

NILM - Negative for Intraepithelial Lesion or Malignancy

In three patients, cytological analysis revealed features of HSIL with prominent koilocytosis (perinuclear halos, nuclear hyperchromasia, and irregular nuclear contours). Morphological verification confirmed CIN II–III, supporting the diagnostic accuracy

of cytology in these cases. HPV genotyping demonstrated oncogenic HPV types 16, 35, 45, 52, and 58, confirming high progression risk and underscoring the need for close clinical surveillance and timely intervention (Table 2).

Table 3 - CIN grade distribution and morphological characteristics

CIN grade	Number of patients (n=40)	Percentage (%)	Nuclear enlargement (%)	Hyperchromasia (%)	Mitoses (%)
CIN I	11	27,5%	0	0	0
CIN II	18	45%	4	4	0
CIN III	9	22,5%	9	9	9

* CIN - Cervical Intraepithelial Neoplasia

Selected clinical cases:

- **Case 1.** A 28-year-old patient presented with a Pap smear result indicating LSIL. HPV genotyping revealed high-risk HPV 16. Histological examination from colposcopy-guided biopsy showed CIN I on the background of cervicitis. No STIs were identified. This case demonstrates concordance between cytology and histology, though the presence of high-risk HPV highlights the need for follow-up.

- **Case 2.** A 31-year-old patient had no cytological abnormalities (NILM). However, HPV genotyping revealed types 31 and 58 (high-risk). Histology confirmed CIN II with chronic cervicitis, and *Gardnerella vaginalis* infection was identified. This case illustrates the limitations of cytology in persistent HPV

infection and underscores the importance of combined evaluation including colposcopy and biopsy.

- **Case 3.** A 25-year-old patient presented with LSIL on cytology. HPV testing revealed multiple high-risk types (HPV 16, 18, 45). Histology diagnosed CIN III (carcinoma in situ) with cervicitis. *Mycoplasma hominis* infection was also present. This case emphasizes the discrepancy between cytology and histology, particularly in HPV co-infections, and the need for a more aggressive management approach in high-risk patients (Table 3).

These findings collectively demonstrate the diagnostic value of an integrated approach (cytology, HPV typing, colposcopy, and histology). In some cases, even low-grade or negative cytological results masked significant histological lesions (up to CIN III/carcinoma in situ).

Table 4 - Diagnostic method comparison in selected cases

Patient	PAP smear results	HPV typing	STIs	Histology
№1	LSIL	HPV 16	negative	CIN I, cervicitis
№2	NILM	HPV 31, 58	Gardnerella vaginalis	CIN II, cervicitis
№3	LSIL	HPV 16, 18, 45	Mycoplasma hominis	CIN III carcinoma in situ), cervicitis

* CIN - Cervical Intraepithelial Neoplasia

LSIL - Low-grade squamous intraepithelial lesion

NILM - Negative for Intraepithelial Lesion or Malignancy

HPV - human papillomavirus

The presented clinical cases were included in the results section to illustrate the diagnostic value of an integrated approach in detecting CIN. These examples demonstrate that Pap smear data alone may be insufficient for an objective assessment of lesion severity. In certain cases, despite low cytological categories (e.g., LSIL or NILM), histological examination revealed more advanced forms of CIN, including carcinoma in situ. This underscores the necessity of combined diagnostics, incorporating cytological, virological, and morphological evaluation for accurate risk stratification and appropriate patient management (Table 4).

The results of this study revealed significant discrepancies between cytological and histological diagnoses in patients with CIN, raising concerns regarding the effectiveness of standard Pap smear-based screening strategies. In 47.5% of patients with cytological diagnoses of LSIL or ASC-US, histological examination confirmed CIN II, CIN III, or carcinoma in situ. Such discrepancies indicate an underestimation of epithelial abnormalities during initial cytological interpretation, which in clinical practice may result in delays in diagnosis and initiation of appropriate treatment.

Moreover, in four patients (10%) with NILM (Negative for Intraepithelial Lesion or Malignancy), histology confirmed CIN I and CIN II. These cases demonstrate the possibility of false-negative cytology results and emphasize the necessity of a combined diagnostic approach that includes HPV testing and colposcopy in addition to cytology.

Similar findings have been reported in large retrospective studies, including one involving 3,798 patients who underwent HPV testing, cytology, and subsequent colposcopic biopsy. According to those data, for CIN I the most common cytological diagnoses were ASC-US (38.2%) and LSIL (36.1%), whereas for CIN II, ASC-US (31.4%) and LSIL (26.6%) also predominated [36]. Thus, moderate lesions may be present even when cytological abnormalities appear minor. For CIN III, HSIL was the most common cytological diagnosis (43.4%), although a substantial proportion of patients presented with milder abnormalities, such as ASC-H (20.6%) and even ASC-US.

Particular attention should be paid to the phenomenon of **undercall**, where CIN II or higher is detected histologically in patients whose cytology results are $\leq$ ASC-US. In the cited study, 373 such cases were identified. Importantly, HPV 16/18 positivity was more frequently associated with undercall ($p < 0.01$), whereas age over 45 years was associated with a lower risk of diagnostic error [36]. Comparable patterns were observed in our study, where histologically significant lesions were found in some patients despite NILM results.

The discrepancies identified in our research confirm the need to reconsider existing approaches to interpreting screening results and emphasize the importance of integrated diagnostic strategies, particularly in high-risk populations. A combination of Pap smear, HPV genotyping, colposcopy, and, when necessary, directed biopsy should be regarded as the

standard of care for patients with borderline cytological results.

Our findings also align with previously published data that highlight the limitations of cytology as a stand-alone method. Cytology, while effective as a first-line screening tool, cannot always provide sufficient sensitivity or specificity for high-grade lesions, particularly in the context of coexisting infections or inflammatory changes. Conversely, histology allows for more reliable detection of key morphological features associated with progression risk, including nuclear atypia, hyperchromasia, and mitotic activity.

In addition, the detection of high-risk HPV types (16, 35, 45, 52, 58) in conjunction with severe morphological atypia underscores the necessity of

incorporating HPV testing into diagnostic algorithms. The combination of HPV typing and histological verification enables more accurate patient stratification, minimizes the likelihood of underdiagnosis, and supports timely therapeutic interventions.

Taken together, these data reinforce the notion that cervical cancer prevention programs must move toward an integrated model that combines cytological, virological, and morphological approaches. Such a strategy not only increases diagnostic accuracy but also improves patient outcomes, particularly in populations with limited access to healthcare resources and high prevalence of HPV infection.

4. Conclusion

The findings of this study underscore the fundamental role of morphological verification in the diagnosis of CIN, particularly in the context of HPV-associated pathology. Despite the advances in virological and cytological screening methods, histological examination remains the most reliable tool for determining the grade of dysplasia and identifying morphological features associated with progression risk, such as nuclear atypia, hyperchromasia, and mitotic activity.

The discrepancies revealed between Pap smear results and histological findings (including cases of CIN III in patients with NILM or LSIL cytology) demonstrate the limitations of isolated cytological diagnostics and emphasize the necessity of a comprehensive diagnostic approach. This approach should include colposcopic monitoring, HPV genotyping, and pathomorphological evaluation.

The presence of high-risk HPV types (16, 35, 45, 52, 58) in combination with pronounced morphological atypia requires special clinical attention, even when cytological findings are of low grade or indeterminate significance.

Thus, the effectiveness of CIN diagnosis and patient management is directly dependent on

multidisciplinary collaboration and standardized morphological interpretation. This is particularly relevant in regions with high HPV prevalence and limited oncological screening resources. The results of this study justify the need to strengthen morphological control over precancerous cervical lesions as a key component of invasive cervical cancer prevention.

Conflict of interest: No conflict of interest declared.

Funding: This research was funded by the Scientific Committee of the Ministry of Science and Higher Education of the Republic of Kazakhstan (grant No. BR24992853, titled "National Program for the Study of HPV with the Development of an Integrated Approach to Effective Diagnosis and Treatment of Precancerous Conditions"). The funding organizations did not participate in the study design, data collection and analysis, decision to publish, or manuscript preparation.

Authors contribution

T.M. Ukybassova, N.K. Kamzayeva, B.A. Ibraimov - Concept and design; N.K. Kamzayeva, M.S. Galym, S.B. Makhambetva, M.S. Galym, D.M. Baktybayeva, K.K. Konrtay, A.G. Toktarkhan, A. Nurgazykyzy - Collection and processing of material; T.M. Ukybassova, N.K. Kamzayeva, B.A. Ibraimov –

Editing; B.A. Ibraimov, M.S. Galym, S.B. Makhambetva,
M.S. Galym, D.M. Baktybayeva, K.K. Konrtay, A.G.
Toktarkhan, A. Nurgazykyzy - Text writing.

References

1. World Health Organization. (2024). WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention: use of dual-stain cytology to triage women after a positive test for human papillomavirus (HPV). World Health Organization. <https://books.google.com/books?hl=ru&lr=&id=IacOEQAQBAJ&oi=fnd&pg=PR5&dq=1.%09World+Health+Organization.+Cervical+cancer.+Geneva:+WHO%3B+2024.+&ots=DnS4Vh7QSC&sig=ABEaGrOiornFxH12L95TlrwKZ1E>
2. Bowden, S. J., Doulgeraki, T., Bouras, E., Markozannes, G., Athanasiou, A., Grout-Smith, H., Kyrgiou, M. (2023). Risk factors for human papillomavirus infection, cervical intraepithelial neoplasia and cervical cancer: an umbrella review and follow-up Mendelian randomisation studies. *BMC medicine*, 21(1), 274. <https://doi.org/10.1186/s12916-023-02965-w>
3. Sabale, U., Reuschenbach, M., Takyar, J., Dhawan, A., Hall, A., Vittal, D., Valente, S. (2025). Epidemiological, economic and humanistic burden of cervical intraepithelial neoplasia in Europe: A systematic literature review. *European Journal of Obstetrics & Gynecology and Reproductive Biology*: X, 25, 100360. <https://doi.org/10.1016/j.eurox.2024.100360>
4. Zhetpisbayeva, I., Rommel, A., Kassymbekova, F., Semenova, Y., Sarmuldayeva, S., Giniyat, A., Glushkova, N. (2024). Cervical cancer trend in the Republic of Kazakhstan and attitudes towards cervical cancer screening in urban and rural areas. *Scientific reports*, 14(1), 13731. <https://doi.org/10.1038/s41598-024-64566-8>
5. Mlynarczyk-Bonikowska, B., Rudnicka, L. (2024). HPV infections—classification, pathogenesis, and potential new therapies. *International Journal of Molecular Sciences*, 25(14), 7616. <https://doi.org/10.3390/ijms25147616>
6. Hampson, I. N. (2022). Effects of the prophylactic HPV vaccines on HPV type prevalence and cervical pathology. *Viruses*, 14(4), 757. <https://doi.org/10.3390/v14040757>
7. Münger, K., Howley, P. M. (2002). Human papillomavirus immortalization and transformation functions. *Virus research*, 89(2), 213-228. [https://doi.org/10.1016/S0168-1702\(02\)00190-9](https://doi.org/10.1016/S0168-1702(02)00190-9)
8. Wang, J. C., Baddock, H. T., Mafi, A., Foe, I. T., Bratkowski, M., Lin, T. Y., Nile, A. H. (2024). Structure of the p53 degradation complex from HPV16. *Nature Communications*, 15(1), 1842. <https://doi.org/10.1038/s41467-024-45920-w>
9. Jeon, S., Lambert, P. F. (1995). Integration of human papillomavirus type 16 DNA into the human genome leads to increased stability of E6 and E7 mRNAs: implications for cervical carcinogenesis. *Proceedings of the National Academy of Sciences*, 92(5), 1654-1658. <https://doi.org/10.1073/pnas.92.5.1654>
10. Pett, M., Coleman, N. (2007). Integration of high-risk human papillomavirus: a key event in cervical carcinogenesis?. *The Journal of Pathology: A Journal of the Pathological Society of Great Britain and Ireland*, 212(4), 356-367. <https://doi.org/10.1002/path.2192>
11. Chen, J. (2015). Signaling pathways in HPV-associated cancers and therapeutic implications. *Reviews in medical virology*, 25, 24-53. <https://doi.org/10.1002/rmv.1823>
12. Höhn, A. K., Brambs, C. E., Hiller, G. G. R., May, D., Schmoeckel, E., Horn, L. C. (2021). 2020 WHO classification of female genital tumors. *Geburtshilfe und Frauenheilkunde*, 81(10), 1145-1153. <https://doi.org/10.1055/a-1545-4279>
13. Board, W. (2020). WHO classification of tumours: female genital tumours.
14. Darragh, T. M., Colgan, T. J., Cox, J. T., Heller, D. S., Henry, M. R., Luff, R. D., Spires, S. (2012). The lower anogenital squamous terminology standardization project for HPV-associated lesions: background and consensus

recommendations from the College of American Pathologists and the American Society for Colposcopy and Cervical Pathology. *Archives of pathology & laboratory medicine*, 136(10), 1266-1297. <https://doi.org/10.5858/arpa.LGT200570>

15. Reuschenbach, M., Wentzensen, N., Dijkstra, M. G., von Knebel Doeberitz, M., Arbyn, M. (2014). p16INK4a immunohistochemistry in cervical biopsy specimens: a systematic review and meta-analysis of the interobserver agreement. *American journal of clinical pathology*, 142(6), 767-772. <https://doi.org/10.1309/AJCP3TPHV4TRIZEK>

16. Vinothini, R. P. V., Bhandari, T. P. S., Saksena, A. R., & Swain, M. (2024). Molecular Classification of Vulvar Squamous Cell Carcinoma and Precursor Lesions Using Immunohistochemistry. *Journal of Colposcopy and Lower Genital Tract Pathology*, 2(2), 65-70. https://doi.org/10.4103/JCLGTP.JCLGTP_9_24

Адам папилломасы вирусы - ассоцияланған патология контексінде жатыр мойнының интраэпителиалды неоплазиясының морфологиялық сипаттамалары

[Ибраимов Б.Ә.](#) ^{1*}, [Үкібасова Т.М.](#) ², [Ғалым М.С.](#) ³, [Махамбетова С.Б.](#) ⁴, [Бактыбаева Д.М.](#) ⁵,
[Қоңыртай Қ.Қ.](#) ⁶, [Қамзаева Н.Қ.](#) ⁷, [Тоқтархан А.Г.](#) ⁸, [Нұрғазықызы А.](#) ⁹

¹ Клиникалық және академиялық зертханалық медицина, патология және генетика кафедрасының патологиялық анатомия бөлімінің меңгерушісі, «University Medical Center» Корпоративтік қоры, Астана, Қазақстан

² Профессор, гинеколог дәрігер, Әйелдер денсаулығының клиникалық академиялық департаменті, «University Medical Center» Корпоративтік қоры, Астана, Қазақстан

³ Гинеколог дәрігер, Әйелдер денсаулығының клиникалық академиялық департаменті, «University Medical Center» Корпоративтік қоры, Астана, Қазақстан

⁴ Гинеколог дәрігер, Әйелдер денсаулығының клиникалық академиялық департаменті, «University Medical Center» Корпоративтік қоры, Астана, Қазақстан

⁵ Гинеколог дәрігер, Әйелдер денсаулығының клиникалық және академиялық департаменті, «University Medical Center» Корпоративтік қоры, Астана, Қазақстан

⁶ Гинеколог, Әйелдер денсаулығының клиникалық академиялық департаменті, «University Medical Center» Корпоративтік қоры, Астана, Қазақстан

⁷ Гинеколог дәрігер, Әйелдер денсаулығының клиникалық академиялық департаменті, «University Medical Center» Корпоративтік қоры, Астана, Қазақстан

⁸ Патолог-анатом дәрігер, Зертханалық медицина, патология және генетика клиникалық және академиялық департаменті, «University Medical Center» Корпоративтік қоры, Астана, Қазақстан

⁹ Патолог-анатом дәрігер, Зертханалық медицина, патология және генетика клиникалық және академиялық департаменті, «University Medical Center» Корпоративтік қоры, Астана, Қазақстан

Түйіндеме

Зерттеудің мақсаты. Әдебиеттерге шолу және клинико-морфологиялық деректерді талдау негізінде адам папилломасы вирусы (АПВ) - ассоцияланған патология контексінде жатыр мойнының интраэпителиалды неоплазиясының (CIN) морфологиялық сипаттамаларын жүйелеу.

Әдістері. Зерттеуге University Medical Center патологиялық анатомия бөлімінде алдын ала қатерлі ісік аурулары бар пациенттерден алынған жатыр мойнының 40 биопсия үлгісі енгізілді. Гистологиялық бағалау гематоксилин-эозин бояуын қолдану арқылы жүргізілді. Талдауға клиникалық және зертханалық деректер енгізілді, соның ішінде цитологиялық зерттеу нәтижелері (Pap-тест), АПВ типтеу және жыныстық жолмен берілетін инфекцияларға (ЖЖБИ) скрининг.

Нәтижелері. Ең жиі анықталған АПВ түрі 16-тип болды (14 жағдай). Екі реттік АПВ - инфекция 9 пациентте тіркелді (мысалы, 16 және 45, 18 және 51), ал 3 пациентте үштік инфекция анықталды. 16 жағдайда АПВ табылмады. CIN-нің жоғары дәрежесі (CIN 2, CIN 3 немесе carcinoma in situ) 40 пациенттің 19-ында (47,5%) анықталды, цитологияда тек төмен дәрежелі зақымданулар (LSIL) немесе атипия (ASC-US) көрсетілгеніне қарамастан. Бұдан басқа, 4 жағдайда (10%) цитология NILM (интраэпителиалды зақымдану немесе қатерлілік белгілері жоқ) болғанымен, гистологиялық зерттеуде CIN I–II анықталды. ЖЖБИ 26 пациентте (65%) анықталды, көбінесе *Gardnerella vaginalis* (55%), содан кейін *Cytomegalovirus* (17,5%), *Candida albicans* (10%) және *Mycoplasma hominis* (7,5%), аралас инфекциялармен қоса. Бұл деректер CIN бар пациенттерде АПВ және қосалқы ЖЖБИ кең таралғанын, сондай-ақ қабыну процестері аясында цитологиялық және гистологиялық нәтижелер арасындағы айтарлықтай айырмашылықтарды көрсетеді.

Қорытынды. Зерттеу цитологиялық скринингтің шектеулерін және морфологиялық, клиникалық және молекулалық әдістерді біріктіретін кешенді диагностикалық стратегиялардың қажеттілігін көрсетеді. CIN-нің морфологиялық критерийлерін стандарттау, әсіресе ВПЧ-ассоциацияланған және қабыну жағдайларында, диагноздың дәлдігін арттыру және пациенттерді оңтайлы басқару үшін аса маңызды.

Түйін сөздер: жатыр мойнының интраэпителиалды неоплазиясы, адам папилломасы вирусы, цитология мен гистология корреляциясы, жыныстық жолмен берілетін инфекциялар, морфология.

Морфологические характеристики цервикальной интраэпителиальной неоплазии в контексте вирус папилломы человека - ассоциированной патологии

[Ибраимов Б.А.](#)^{1*}, [Укыбасова Т.М.](#)², [Галым М.С.](#)³, [Махамбетова С.Б.](#)⁴,
[Бактыбаева Д.М.](#)⁵, [Конртай К.К.](#)⁶, [Камзаева Н.К.](#)⁷, [Токтархан А.Г.](#)⁸, [Нургязыкызы А.](#)⁹

¹ Заведующий отделом патологической анатомии Клинического и академического департамента лабораторной медицины, патологии и генетики, Корпоративный фонд «University Medical Center», Астана, Казахстан

² Профессор, врач гинеколог, Клинический академический департамент женского здоровья, Корпоративный фонд «University Medical Center», Астана, Казахстан

³ Врач гинеколог, Клинический академический департамент женского здоровья, Корпоративный фонд «University Medical Center», Астана, Казахстан

⁴ Врач гинеколог, Клинический академический департамент женского здоровья, Корпоративный фонд «University Medical Center», Астана, Казахстан

⁵ Врач гинеколог, Клинический академический департамент женского здоровья, Корпоративный фонд «University Medical Center», Астана, Казахстан

⁶ Врач гинеколог, Клинический академический департамент женского здоровья, Корпоративный фонд «University Medical Center», Астана, Казахстан

⁷ Врач гинеколог, Клинический академический департамент женского здоровья, Корпоративный фонд «University Medical Center», Астана, Казахстан

⁸ Врач-патолог анатом Клинического и академического департамента лабораторной медицины, патологии и генетики, Корпоративный фонд «University Medical Center», Астана, Казахстан

⁹ Врач-патолог анатом Клинического и академического департамента лабораторной медицины, патологии и генетики, Корпоративный фонд «University Medical Center», Астана, Казахстан

Абстракт

Цель исследования. Систематизировать морфологические характеристики цервикальной интраэпителиальной неоплазии (CIN) в контексте вирус папилломы человека (ВПЧ) - ассоциированной патологии на основе обзора литературы и анализа клинико-морфологических данных.

Методы. В исследование включено 40 образцов биопсии шейки матки, полученных у пациенток с предраковыми заболеваниями шейки матки, обследованных в отделении патологической анатомии University Medical Center. Гистологическая оценка выполнялась с использованием окраски гематоксилин-эозином. В анализ были интегрированы клинические и лабораторные данные, включая результаты цитологического исследования (Пар-тест), типирование ВПЧ и скрининг на инфекции, передаваемые половым путем (ИППП).

Результаты. Наиболее часто выявлялся ВПЧ 16-го типа (14 случаев). Двойные ВПЧ-инфекции отмечены у 9 пациенток (например, 16 и 45, 18 и 51), у 3 пациенток зарегистрированы тройные инфекции. В 16 случаях ВПЧ не был обнаружен. Высокая степень CIN (CIN 2, CIN 3 или carcinoma in situ) диагностирована у 19 из 40 пациенток (47,5%), несмотря на то, что цитология показала только низкостепенные поражения (LSIL) или атипичию неуточненного значения (ASC-US). Кроме того, в 4 случаях (10%) при цитологии NILM (отсутствие признаков интраэпителиального поражения или злокачественности) гистологически выявлен CIN I–II. ИППП диагностированы у 26 пациенток (65%), преимущественно *Gardnerella vaginalis* (55%), далее Cytomegalovirus (17,5%), *Candida albicans* (10%) и *Mycoplasma hominis* (7,5%), включая смешанные инфекции. Эти данные свидетельствуют о высокой распространенности ВПЧ и сопутствующих ИППП у пациенток с CIN, а также о значительных расхождениях между цитологическими и гистологическими результатами, особенно на фоне воспалительных процессов.

Выводы. Исследование подчеркивает ограничения цитологического скрининга и необходимость комплексных диагностических стратегий, объединяющих морфологические, клинические и молекулярные методы. Стандартизация морфологических критериев CIN особенно важна в условиях ВПЧ-ассоциированных и воспалительных состояний для повышения точности диагностики и оптимизации ведения пациенток.

Ключевые слова: цервикальная интраэпителиальная неоплазия, ВПЧ, корреляция цитологии и гистологии, инфекции, передаваемые половым путем, морфология.