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ANALYSIS OF HPV GENOTYPE DISTRIBUTION, VIRAL LOAD PROFILES, AND THEIR RELATIONSHIP WITH CERVICAL PATHOLOGY AMONG WOMEN IN SAMARKAND REGION (2023-2025)

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Abstract

Introduction: Persistent infection with high-risk oncogenic human papillomavirus (HPV) is the primary cause of cervical cancer development.

Objective: To evaluate the prevalence of various HPV genotypes, describe genotype-specific viral load patterns, and determine their relationship with patient age and cervical cytological changes among women in the Samarkand region.

Methods: In a cross-sectional study (2023-2025), cervical epithelial samples from 535 women (aged 19-56 years) were analyzed. Genotyping of 21 HPV types and quantification of viral load (expressed in lg copies of DNA/10^5 cells) were performed using real-time PCR. Cytological status was classified according to The Bethesda System (TBS, 2014) in cohorts with monoinfection (n=73) and mixed infection (n=20).

Results: Out of 116 HPV-positive cases, HPV 16 was unconditionally dominant (24%). An atypically low prevalence of HPV 18 (3%) was observed alongside a high detection rate of non-vaccine types: HPV 56 (6%), 51 (5%), and 58 (4%). No statistically significant correlation was found between patient age and viral load ($p>0.05$). A significant overall association was revealed between HPV genotype and cytological status ($\chi^2=97.06$; df=68; $p=0.012$). HPV 58 demonstrated the highest pathogenetic potential (OR=12.11; 80% of cases were ASC-US, 20% were ASC-H) and was never detected in normal cytology (NILM). No direct linear correlation was found between viral load level and lesion severity: peak loads were recorded in NILM cases,

whereas the only severe case (HSIL, associated with HPV 68) presented with a low viral load (2.7 lg copies/10^5 cells).

Conclusion: The regional epidemiological profile is determined by the dominance of HPV 16 and a high circulation of high-risk non-vaccine strains (56, 51, 58). Viral load exhibits immense genotype-specific variability and does not directly correlate with the severity of cytological changes, highlighting the necessity of integrating multi-genotype PCR testing and cytological screening.

Keywords: Human papillomavirus, The Bethesda System, Mixed infection, Samarkand region, liquid-based cytology.

Introduction / Relevance

Human papillomavirus infection is one of the most common sexually transmitted infections and represents a leading issue in modern gynecologic oncology. Of the more than 40 HPV types capable of infecting the mucous membranes of the anogenital tract, some belong to high oncogenic risk types, the persistence of which is the essential prerequisite for the development of precancerous lesions and cervical cancer [1, 2]. The most significant role in carcinogenesis is played by the oncogenic proteins E6 and E7, which disrupt cell cycle regulation, apoptosis mechanisms, and the genomic stability of infected cells [3, 4, 5]. Although most HPV infections are transient and cleared by the immune system within approximately two years, in a subset of women, the infection becomes persistent, creating conditions for the sequential formation of cervical intraepithelial neoplasia and subsequent malignancy [1, 6].

HPV persistence is determined not only by the properties of the virus itself but also by a combination of host organism factors and the local microenvironment. The type and variant of HPV, the state of the immune system, host genetic features, hormonal and metabolic factors, smoking, co-insions, reproductive history characteristics, and other external influences are of substantial significance [7, 8]. In recent years, increasing attention has also been paid to epigenetic mechanisms, alterations in gene expression, and regulatory non-coding RNAs that may participate in the transition from persistent infection to neoplastic transformation [9, 10]. Chromosomal instability and aneuploidy are also considered important components in the progression of HPV-associated carcinogenesis [11].

Of particular importance is the pronounced genotypic heterogeneity of HPV and differences in the structure of circulating genotypes across distinct geographic regions and populations. In various countries and regions, alongside HPV 16 and HPV 18 (traditionally viewed as the primary highly oncogenic types), a significant presence of HPV 31, 33, 35, 45, 51, 52, 56, 58, and other genotypes is detected [2, 8, 12]. The ratio of individual types can vary substantially depending on the population, the age of the screened women, and screening and vaccination characteristics [13, 14]. For Central Asian countries, this issue is of particular interest due to the insufficient representation of regional molecular epidemiological data.

An important quantitative metric of HPV infection is viral load. However, modern studies show that its relationship with the severity of cytological and morphological changes is not always linear. A high concentration of viral DNA can be observed both in the absence of pronounced cytological changes and in lesions of varying severity. On the other hand, during the progression of the neoplastic process, changes in the ratio of episomal and integrated forms of viral DNA can potentially be accompanied by alterations in the detectable viral load [3, 9]. Therefore, it is appropriate to consider viral load not as an independent diagnostic criterion for the degree of

injury, but as an additional characteristic of the infection combined with genotyping and cytological evaluation.

The presence of multiple HPV infections introduces additional complexity. The simultaneous circulation of several genotypes may be accompanied by varying quantitative ratios of viral DNA, including the dominance of a single genotype, similar levels across multiple types, or a pronounced difference in their viral loads. The genotypic profile and the specific combination of separate types can affect infection persistence and the development of cervical pathology [8, 12]. Therefore, simply establishing an HPV-positive status is insufficient for a full characterization of the infection; an assessment of its genotypic structure and, when possible, the quantitative parameters of each detected genotype is required.

Modern research also emphasizes the potential role of the vaginal and cervical microbiome in the establishment of persistent HPV infection and the development of neoplastic changes. In a physiological microbiome state, representatives of the genus *Lactobacillus*, particularly *Lactobacillus crispatus*, play a significant role, whereas a decrease in their abundance and the development of dysbiotic states, including bacterial vaginosis, are associated with alterations in the local immune response and a higher rate of HPV persistence. The community state types framework, established via advanced microbiome analysis methods, has enabled a more detailed characterization of vaginal microbial community compositions. At the same time, the causal direction between microbiome changes, HPV persistence, and the development of cervical neoplasia has not yet been definitively established [15, 16]. Nonetheless, experimental and clinical studies point to the possible participation of the microbiome in immune regulation, viral clearance, and the formation of conditions favoring the progression of cervical lesions. This domain is viewed as promising for further study of HPV persistence mechanisms and the development of additional preventive approaches.

Prevention of HPV-associated diseases relies primarily on vaccination and organized screening. HPV vaccination significantly reduces the risk of infection by the most critical oncogenic genotypes and their related precancerous lesions [6, 13, 17]. However, the structure of circulating genotypes in various populations may differ from the spectrum of types included in vaccines. Consequently, continuous molecular epidemiological monitoring is vital for evaluating the efficacy of prevention programs and refining regional screening and vaccination strategies [13, 18, 19]. This is especially relevant for countries with developing prevention systems, where a combination of vaccination, HPV testing, and cytological screening can substantially reduce the burden of diseases associated with HPV [6, 20].

For Uzbekistan, this problem is of particular relevance because regional data regarding the prevalence of individual HPV genotypes, their viral load characteristics, and their relationship with cervical cytological changes remain limited. Available studies indicate a need to expand molecular epidemiological research while accounting for regional population characteristics [20, 21, 22, 23, 24]. Yet, not only the frequency of individual highly oncogenic genotypes but also their combinations in multiple infections, quantitative viral load characteristics, and genotype distribution relative to the cytological state of the cervix remain insufficiently studied [25, 26, 27].

Materials and methods

The primary aim of this study was to evaluate the prevalence of various Human Papillomavirus (HPV) genotypes among women in the Samarkand region, describe genotype-specific viral load patterns in mono- and mixed infections, and determine their relationship with patient age and cervical cytological changes.

Study design and sample characteristics

A cross-sectional observational clinical-molecular study with a retrospective analysis of archival cervical smear material was conducted. The study was carried out using the database of the private clinic "VERSUS NEXT" LLC (Address: 38/1 Shahrisabz St., Samarkand, Republic of Uzbekistan) and spanned the period between January 2023 and December 2025.

The study object comprised verified biological material (scrappings/smears from the cervical canal) obtained from n=535 women aged 19 to 56 years (mean age: 34.2±7.4 years; median: 34.0; IQR: 28.0-40.0 years). Participants were residents of Samarkand city and eight districts of the Samarkand region, including Pastdargom, Samarkand, Ishtikhon, Payariq, Kattaqo‘rg‘on, Jomboy, Narpay, and Urgut.

Inclusion Criteria: Initial screening involved all n=535 women, from whom 116 HPV-positive samples were identified and selected for deep analysis. Matching cytological data were available for n= 93patients, who formed the final cohort for evaluating relationships between viral load and cytological status.

Exclusion Criteria: Pregnancy at the time of examination, prior cervical conization or surgical treatment for cervical neoplasia, a history of cervical malignancies, insufficient quantity or unsatisfactory quality of biological material, and the absence of results from any stage of the examination.

Processes, interventions and comparisons

Biological material sampling was performed from the cervical canal, ectocervix, and transformation zone using a single-use specialized cervical brush (Cervex-Brush).

HPV Genotyping and Quantification

DNA extraction and PCR diagnostics were carried out using Real-Time Polymerase Chain Reaction (Real-Time PCR) on the "HPV quant-21" diagnostic kit ("DNA-Technology TS" LLC, Russia). The panel differentiated 21 HPV genotypes:

High oncogenic risk: HPV 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, and 82.

Low oncogenic risk: HPV 6, 11, and 44.

Patients were compared based on the nature of the infection: monoinfection (n=73) vs. mixed infection (n=20). Evaluation of sample collection adequacy and viral load normalization were performed using a sample control amplification mix (SRC—sample received control). The viral load (VL) was calculated relative to host cell count and expressed logarithmically as decimal logarithm of HPV DNA copies per 10^5host cells (lgcopies/105cells) using the formula:

$$\mathrm{VL} = \lg \frac{N_{\mathrm{HPV}}}{N_{\mathrm{SRC}}} \times 10^5$$

where:

NHPV-is the number of HPV DNA copies in the reaction; NSRC-is the number of host organism cells (calculated by the SRC DNA level).

Viral load was presented in logarithmic units (lg copies of HPV DNA per 10^5 host cells). Logarithmic transformation was applied to minimize the impact of severe right-skewed distribution asymmetry and the wide range of initial quantitative values, as well as to improve metric comparability across patients and different HPV genotypes. In monoinfections, the resulting value was treated as the viral load of that single genotype. In mixed infections, viral load was determined separately for each detected genotype, allowing evaluation of the quantitative

ratios of multi-type infection components and identification of the genotype with the maximum viral load within a specific infectious profile [28, 29].

Cytological Slide Preparation and Examination

Slide preparation was carried out using conventional and liquid-based cytology (LBC). For LBC, the automated CellPrep processor (Biomed, South Korea) was utilized according to the manufacturer's protocol. For conventional cytological examination, smears were stained using the classic Papanicolaou technique (Pap stain).

Cytomorphological analysis was performed on squamous and glandular cervical epithelial cellular material using a light microscope.

Initial slide screening was performed at a standard diagnostic magnification of ×400 (objective×40, ocular×10). For detailed examination of nuclear structures and chromatin distribution patterns, ×1000 magnification with oil immersion was applied.

Microscopic assessment evaluated the morphological characteristics of the cellular nuclear apparatus, including:

- The severity of karyomegaly and alterations in the nucleocytoplasmic ratio;
- Nuclear size, shape, and spatial arrangement;
- Chromatin texture and degree of clumping;
- Chromatin architecture and distribution uniformity;
- Clarity, thickness, and regularity of nuclear membrane (karyolemma) contours;
- Presence and character of nuclear structures and inclusions;
- Presence of specific cytomorphological phenomena indicative of viral injury, including the koilocytic halo, herpetic molding, and the "ground-glass" effect.

Special attention was paid to signs of an altered nucleocytoplasmic ratio and changes in chromatin and nuclear membrane structures, as these characteristics are highly critical when cytologically evaluating epithelial lesion severity [28, 30, 31, 32].

All cytological slides were evaluated by qualified cytopathologists with mandatory quality control for smear adequacy.

Interpretation and categorization of results were performed in strict compliance with The Bethesda System (TBS, 2014) into five categories:

1. Negative for Intraepithelial Lesion or Malignancy (NILM)
2. Atypical Squamous Cells of Undetermined Significance (ASC-US)
3. Low-grade Squamous Intraepithelial Lesion (LSIL)
4. Atypical Squamous Cells, cannot exclude HSIL (ASC-H)
5. High-grade Squamous Intraepithelial Lesion (HSIL)

NILM corresponded to the absence of cytological markers of intraepithelial lesions or malignant processes. ASC-US characterized the presence of atypical squamous cells of undetermined significance. LSIL corresponded to a low-grade squamous intraepithelial lesion. The ASC-H category was applied upon identifying atypical cells where a high-grade lesion could not be ruled out. HSIL corresponded to a high-grade squamous intraepithelial lesion [29,30,33,34].

Cytological categories were utilized to assess the association of quantitative viral load with the nature and severity of cervical epithelial cell changes.

Statistical analysis

Statistical data processing was performed using IBM SPSS Statistics (version 29.0, IBM Corp., Armonk, NY, USA, 2023) and R software packages (version 4.4.2, R Foundation for Statistical Computing, Vienna, Austria, 2024). Quantitative metrics were expressed as arithmetic

mean ± standard deviation (M±SD), or median and interquartile range (Me; IQR) after evaluation of distribution patterns via the Shapiro-Wilk test.

Correlation Testing: Pearson's linear correlation coefficient (r) was applied for normally distributed data, and Spearman's rank correlation coefficient (ρ) was implemented for non-normal or skewed distributions to assess the relationship between age and viral load.

Group Comparisons: The Mann-Whitney U test was performed to compare viral loads between two independent groups, while the Kruskal-Walli's test was used for comparisons involving more than two groups, followed by Dunn's post-hoc test with adjustment for multiple comparisons.

Categorical Associations: Proportional distributions and contingency tables were evaluated using Pearson's χ^2test or Fisher's exact test. Odds ratios (OR) with 95% confidence intervals (95% CI) were calculated to evaluate the strength of clinical association. To control the False Discovery Rate (FDR) during multiple comparisons, the Benjamini-Hochberg correction was implemented. Differences were considered statistically significant at p<0.05. [35, 36, 37].

Note on Power Calculation: A formal sample size power calculation was not executed prior to enrollment due to the descriptive, cross-sectional nature of this regional molecular-epidemiological screening protocol, which relied on the comprehensive registration of all eligible archiving materials during the target 2023-2025 window.

Ethical Considerations

The study was conducted in accordance with the principles of the Declaration of Helsinki. The research protocol was officially reviewed and approved by the Local Bioethics Committee of Samarkand State University named after Sharof Rashidov (Protocol No. 8, 2026). Informed consent was obtained from all individual participants included in the study.

Results

Within the overall HPV-positive cohort (n=116), the structure of the proportional distribution of specific strains for 2023-2025 was analyzed (Table 1, Fig. 1, Fig. 2).

Table 1. Distribution and proportion of identified HPV types in the Samarkand region (n=116)

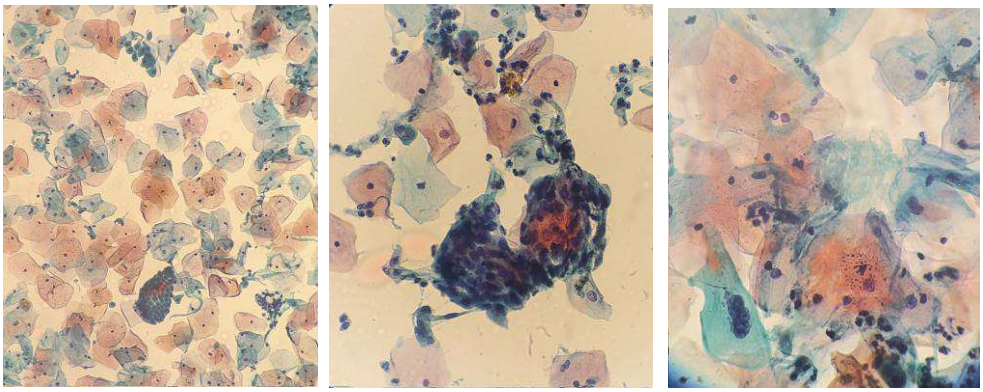
HPV Genotype	*Total, n*	*NILM, n (%)*	*ASC-US, n (%)*	*ASC-H, n (%)*	*LSIL, n (%)*	*HSIL, n (%)*
HPV 16	15	8 (53.3)	2 (13.3)	0 (0)	5 (33.3)	0 (0)
HPV 51	4	1 (25.0)	2 (50.0)	0 (0)	1 (25.0)	0 (0)
HPV 56	8	5 (62.5)	2 (25.0)	0 (0)	1 (12.5)	0 (0)
HPV 52	3	1 (33.3)	1 (33.3)	0 (0)	1 (33.3)	0 (0)
HPV 39	2	1 (50.0)	1 (50.0)	0 (0)	0 (0)	0 (0)
HPV 68	2	0 (0)	0 (0)	0 (0)	1 (50.0)	1 (50.0)
HPV 45	5	4 (80.0)	0 (0)	0 (0)	1 (20.0)	0 (0)
HPV 66	1	1 (100.0)	0 (0)	0 (0)	0 (0)	0 (0)
HPV 11	2	1 (50.0)	1 (50.0)	0 (0)	0 (0)	0 (0)
HPV 18	1	1 (100.0)	0 (0)	0 (0)	0 (0)	0 (0)
HPV 44	6	3 (50.0)	1 (16.7)	0 (0)	2 (33.3)	0 (0)
HPV 73	2	1 (50.0)	0 (0)	1 (50.0)	0 (0)	0 (0)
HPV 6	3	2 (66.7)	0 (0)	0 (0)	1 (33.3)	0 (0)
HPV 53	5	4 (80.0)	0 (0)	0 (0)	1 (20.0)	0 (0)
HPV 58	5	0 (0)	4 (80.0)	1 (20.0)	0 (0)	0 (0)

HPV 35	1	1 (100.0)	0 (0)	0 (0)	0 (0)	0 (0)
HPV 33	2	0 (0)	1 (50.0)	0 (0)	1 (50.0)	0 (0)
Mixed infections	20	11 (55.0)	6 (30.0)	1 (5.0)	2 (10.0)	0 (0)

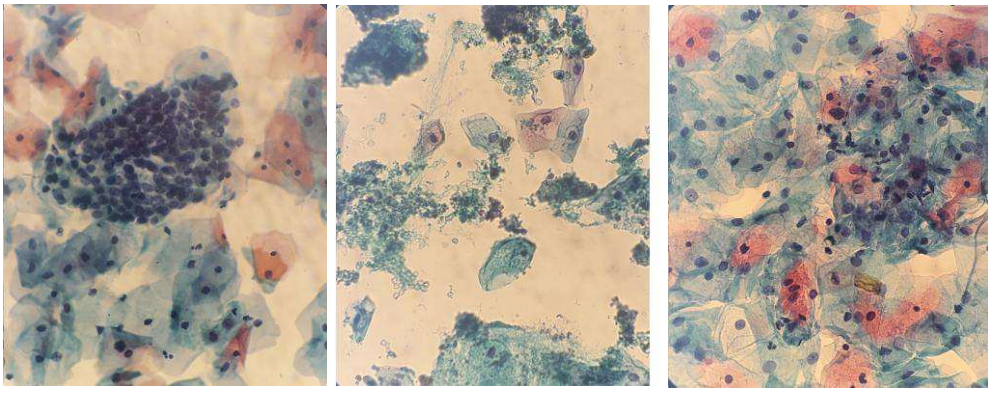
Note: *Percentages in each row are calculated from the total number of women with the corresponding genotype/infection pattern. NILM - Negative for Intraepithelial Lesion or Malignancy; ASC-US - Atypical Squamous Cells of Undetermined Significance; ASC-H - Atypical Squamous Cells, cannot exclude High-grade squamous intraepithelial lesion; LSIL - Low-grade Squamous Intraepithelial Lesion; HSIL - High-grade Squamous Intraepithelial Lesion.*

In the investigated group of women with identified HPV infection, HPV 16 (n=15), HPV 56 (n=8), HPV 44 (n=6), and HPV 45, HPV 53, and HPV 58 (n=5 each) were the most frequently encountered within the cytological monoinfection subgroup. Thus, the cytologically significant spectrum of infection was characterized by a predominance of HPV 16, though genotypes 56, 44, 45, 53, and 58 also maintained substantial representation.

For HPV 16, preferential detection was noted in the absence of cytological signs of a lesion: NILM was registered in 8 out of 15 women (53.3%). Concurrently, LSIL was detected in 5 patients (33.3%), and ASC-US in 2 (13.3%). Consequently, among women with HPV 16 monoinfection, two-fifths of cases were accompanied by cytological changes of varying severity, while HSIL and ASC-H were not recorded in this group. These findings confirm the broad presence of HPV 16 both among women without cytological changes and in low-grade lesions. An interesting profile was revealed for HPV 58: all 5 cases fell into pathological categories of cytological status-4 (80.0%) were ASC-US and 1 (20.0%) was ASC-H; NILM and LSIL were entirely absent.



A **B** **C**



D **E** **F**

Figure 1. Cytomorphological spectrum of liquid-based cervical cytology (CellPrep, Pap stain, ×400): *(A) Normal superficial/intermediate squamous epithelium with glandular cells (left) and metaplastic cells (right); (B) Hyperchromatic crowded cell group (HCG) categorized as ASC-US;) (C) Inflammatory reactive nuclear changes with irregular contours; (D) Atypical glandular cells (AGC) showing loss of normal honeycomb architecture and nuclear crowding; (E) Classical cytopathic effect of HPV (koilocytosis) with distinct perinuclear halo. Pseudohyperchromia induced by dense coccobacillus colonization.; (F) Severe cytolysis with naked nuclei, displaying ASC-US (12 o'clock) and HSIL (8 o'clock) features.*

This forms the most pronounced concentration of atypical shifts among the studied monoinfections for HPV 58. However, due to the small sample size (n=5), this result should be considered an observed trend rather than definitive proof of standalone oncogenic risk for the genotype. For HPV 68, the absence of NILM was likewise noted: one case corresponded to LSIL (50.0%) and the second to HSIL (50.0%). Thus, both identified cases of HPV 68 were accompanied by cytological lesions.

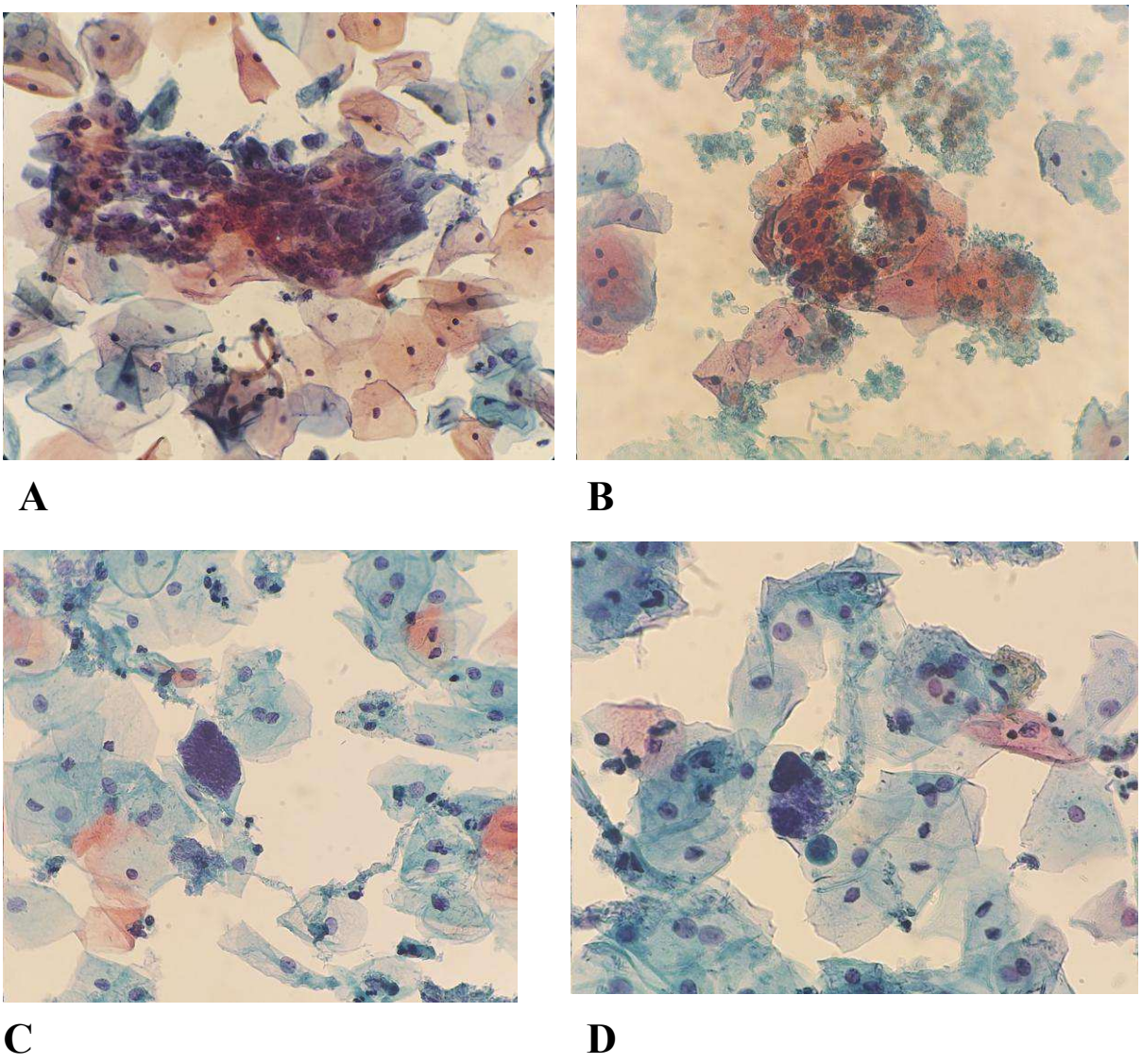


Figure 2. Differential diagnosis of complex intraepithelial lesions and infectious patterns (CellPrep, Pap stain, ×400)*:(A) A three-dimensional hyperchromatic crowded group*

(HCG) with pronounced nuclear overlapping and loss of polarity is visualized in the center of the field of view. A monolayer of mature superficial and intermediate squamous epithelial cells is observed at the periphery. ASC-US; ***(B)*** *A conglomerate of squamous epithelial cells heavily colonized by coccobacilli is visualized in the center. Massive bacterial adhesion and microflora layering create an effect of false hyperchromasia and optical density of the group, mimicking atypical changes while preserving the baseline monomorphic structure of the cell nuclei;* ***(C)*** *True clue cell masking underlying squamous atypia (ASC-US/LSIL) due to bacterial dysbiosis;* ***(D)*** *HSV-induced cytopathic effect with nuclear molding and ground-glass chromatin appearance.*

The presence of a single HSIL case is particularly important. However, given the total n=2, statistical and clinical interpretation is limited; thus, concluding a high association between HPV 68 and HSIL solely based on this table is impossible. For HPV 33, both cases were also accompanied by cytological status modifications: one was ASC-US (50.0%) and the other was LSIL (50.0%). A similar, though less pronounced trend was observed for HPV 73: one case of NILM and one of ASC-H. These outcomes are of interest for further study but require confirmation in a larger cohort.

Regarding HPV 51, out of 4 cases, only one (25.0%) presented with NILM, whereas two women (50.0%) presented with ASC-US and one (25.0%) with LSIL. Thus, 75% of cases of this monoinfection were accompanied by cytological alterations. For HPV 52, the distribution was uniform: one case (33.3%) each for NILM, ASC-US, and LSIL. For HPV 56, NILM predominated-5 out of 8 cases (62.5%), while ASC-US was found in 2 (25.0%) and LSIL in 1 (12.5%). For HPV 44, half of the cases (50.0%) matched NILM, 16.7% matched ASC-US, and 33.3% matched LSIL. Thus, despite the absence of ASC-H and HSIL, one-third of HPV 44 cases were accompanied by LSIL. For HPV 45 and HPV 53, a similar profile was seen: most cases occurred in NILM-80.0% and 80.0% respectively, while LSIL was detected in 20.0% of cases. Low-risk genotypes also demonstrated variations in cytological profiles. For HPV 6, NILM was noted in 66.7% of cases and LSIL in 33.3%. For HPV 11, one case each was distributed to NILM and ASC-US. Crucially, the presence of low-risk genotypes in select LSIL cases should not be interpreted as proof of their independent capacity to induce precancerous alterations, since cytological changes may be driven by confounding factors or undetected genotypes. The 20 cases of mixed infection merit distinct attention. In this group, NILM was registered in 11 women (55.0%), ASC-US in 6 (30.0%), ASC-H in 1 (5.0%), and LSIL in 2 (10.0%); HSIL was not detected.

Consequently, 45.0% of mixed infections were accompanied by cytological shifts, with 5.0% falling into the ASC-H category. Overall, the distribution of mixed infections was characterized by a predominance of NILM. This is important for data interpretation: the mere presence of multiple HPV genotypes cannot be viewed as an unambiguous marker of more severe cytological injury.

In summary, Table 1 displays an inhomogeneous link between separate HPV genotypes and cytological status. For a subset of genotypes-primarily HPV 58, HPV 68, and HPV 33-a high proportion of pathological cytological categories was recorded in this sample. Simultaneously, HPV 16, despite its well-known clinical significance, was detected predominantly in NILM and LSIL, underscoring the lack of a direct relationship between the fact of detecting a specific genotype and the presence of a cytological lesion. Crucially, NILM occurred across nearly all of the most widespread genotypes, including HPV 16, 56, 44, 45, and 53. This indicates that finding HPV in itself is not the equivalent of having a precancerous lesion; clinical evaluation must integrate cytology, infection persistence, genotype, viral load, and other risk factors. Notably, HSIL was identified in only a single case-with HPV 68, whereas for HPV 16, 18, 33, 35, 44, 45,

51, 52, 53, 56, and 58, HSIL was not recorded in the presented sample. This reinforces that drawing conclusions about the link of individual genotypes to HSIL based on this sample is statistically premature.

Analysis of HPV mapping across districts revealed zones of elevated oncogenic risk (Table 2).

Table 2. Distribution of HPV cases across districts of the Samarkand region (2024-2025)

District / City	*Total Cases (n=116)*	*Proportion (%)*	*Dominant Type*	*High-Risk Genotypes*	*Low-Risk Genotypes*
Samarkand City	44	38%	Type 16 (8 cases)	31, 39, 45, 51, 52, 53, 56, 68	6, 11, 44
Pastdargom District	25	22%	Type 16 (10 cases)	33, 45, 51, 56, 58, 82	6, 11
Samarkand District	22	19%	Type 16 (6 cases)	31, 35, 45, 51, 52, 59, 68	6, 44
Ishtikhon District	8	7%	Mixed types	16, 31, 52, 53, 56, 73	44
Payariq District	5	4%	Mixed types	16, 35, 56, 68	6
Kattaqo'rg'on District	5	4%	Mixed types	16, 31, 56, 66	11
Jomboy District	3	3%	Mixed types	16, 53, 56	-
Narpay District	3	3%	Mixed types	51, 53, 58	-
Urgut District	1	1%	Type 66	66	-

Note: *NILM - Negative for Intraepithelial Lesion or Malignancy; ASC-US - Atypical Squamous Cells of Undetermined Significance; ASC-H - Atypical Squamous Cells, cannot exclude High-grade squamous intraepithelial lesion; LSIL - Low-grade Squamous Intraepithelial Lesion; HSIL - High-grade Squamous Intraepithelial Lesion. Viral load is presented in lg copies of HPV DNA per 10^5 cells.*

The highest infectivity indicators were registered in Samarkand city (38%) and Pastdargom district (22%). In Samarkand city, the greatest viral rotation was noted (20 types identified). However, Pastdargom district represents a zone of critical attention, since the highest concentration of the most aggressive type 16 was fixed there (10 cases, or 40% within the district). The low number of cases in remote districts (Jomboy, Narpay, Urgut) combined with the exclusive presence of high-risk types there indicates that screening in these regions is primarily accessed by symptomatic patients.

The mean age of the examined women was 34.2±7.4 years (median 34.0; IQR 28.0-40.0 years). The mean quantitative viral load was 4.58±1.62 lgcopies/10^5 cells (median 4.50 lg copies/10^5 cells). Correlation analysis did not find a statistically significant link between patient age and the quantitative level of viral load. Pearson's correlation coefficient was $r=-0.054$ ($p=0.578$), and Spearman's rank coefficient was $\rho=-0.049$ ($p=0.612$). High viral load values were registered across all age groups: for instance, in a 28-year-old patient with HPV 31 monoinfection, the load was 6.5 lg copies/10^5 cells, while in a 43-year-old woman with HPV 16, it reached 7.3 lg copies/10^5 cells.

Thus, age in itself is not a factor predetermining HPV viral expression. Among 93 fully evaluated patients, no pathological epithelial shifts were detected in 46 (49.4%) (NILM category).

Pathological cytological categories were distributed as follows: ASC-US 24.7% (n=23), LSIL 21.5% (n=20), HSIL 1.0% (n=1), and ASC-H 3.4% (n=3). Stratification of age and viral load for monoinfections (n=73) is presented in Table 3 and Fig.3.

Table 3. Comparison of age, cytology, and viral load in HPV monoinfections (n = 73)

HPV Genotype	*Cytological Status (TBS)*	*Age, years*	*Viral Load, lg copies/10^5 cells*
HPV 16	NILM	24; 26; 43; 45; 30; 35	2.5; 2.5; 7.3; 5.6; 6.3; 3.9
	ASC-US	25; 28	7.0; 7.2
	LSIL	31; 41; 45; 59; 34; 45; 39	2.2; 7.7; 6.5; 6.0; 4.7; 5.0; 4.7
HPV 31	NILM	28; 33; 39	6.5; 2.7; 3.0
	ASC-US	40; 36	6.8; 2.8
	LSIL	24	6.1
HPV 56	NILM	39; 41; 27; 40; 30	4.4; 5.6; 3.4; 2.6; 2.9
	ASC-US	28	2.7
	LSIL	44; 37	3.5; 3.5
HPV 58	ASC-US	40; 40; 30; 39	7.4; 7.4; 3.0; 2.43
	ASC-H	46	4.5
HPV 44	NILM	29; 39; 31	3.8; 4.7; 4.5
	ASC-US	33	3.2
	ASC-H	49	4.9
	LSIL	28	4.0
HPV 51	NILM	38	3.2
	ASC-US	25; 36	3.08; 4.6
	LSIL	29	3.5
HPV 45	NILM	50; 35; 44; 25	4.0; 5.4; 3.0; 5.89
	LSIL	33	4.7
HPV 53	NILM	27; 51; 28; 26	3.8; 4.1; 3.5; 2.4
	LSIL	36	4.9
HPV 52	NILM	20; 30	3.0; 5.1
	ASC-US	37	6.9
HPV 6	NILM	52; 31	3.5; 3.5
	LSIL	29	8.0
HPV 33	ASC-US	34	4.65
	ASC-H	33	6.1
HPV 68	LSIL	52	4.3
	HSIL	44	2.7
HPV 73	NILM	28	2.5
	ASC-H	44	6.5
HPV 11	NILM	28	2.29
	ASC-US	25	1.77
HPV 39	NILM	35	3.9
	ASC-US	32	4.2
HPV 18	NILM	41	2.3

HPV 35	NILM	23	5.9
HPV 66	NILM	31	5.9

Note: *TBS - The Bethesda System; NILM - Negative for Intraepithelial Lesion or Malignancy; ASC-US - Atypical Squamous Cells of Undetermined Significance; ASC-H - Atypical Squamous Cells, cannot exclude HSIL; LSIL - Low-grade Squamous Intraepithelial Lesion; HSIL - High-grade Squamous Intraepithelial Lesion. lg copies/10^5 cells - decimal logarithm of HPV DNA copies per 10^5 human cells. Individual data points for age and viral load correspond sequentially to each patient and are separated by semicolons (;).*

The data demonstrated immense intra-type variability. For HPV 16, the range within the NILM group was 2.5-7.3 lg copies/10^5 cells, and in the LSIL group 2.2-7.7 lg copies/10^5 cells (maximum in a 41-year-old patient). The highest overall viral load was registered for the low oncogenic risk type HPV 6 (8.0 lg copies/10^5 cells in a 29-year-old patient with LSIL).

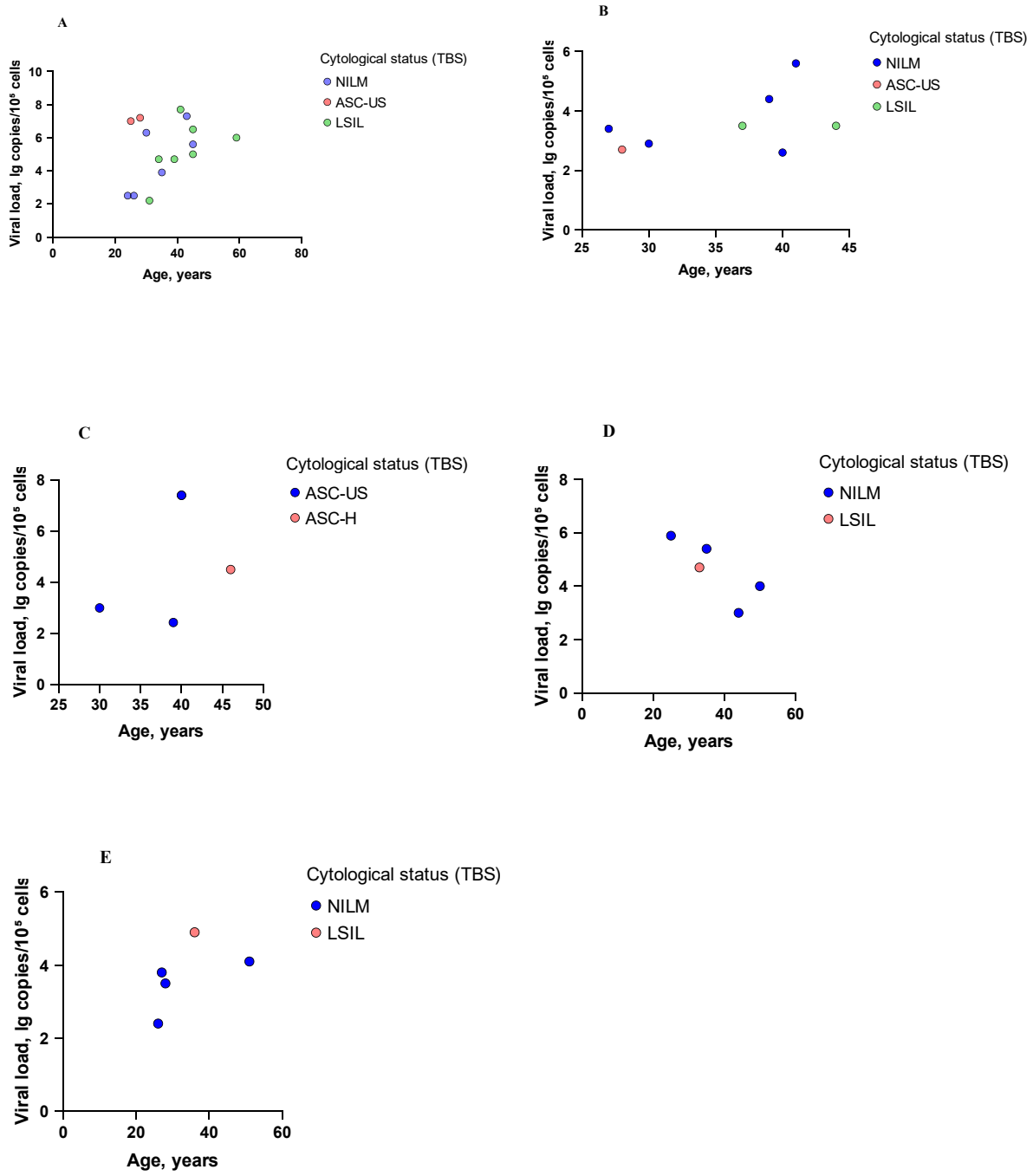


Figure 3. Relationship between viral load and patient age depending on cytological status (according to The Bethesda System, TBS).*Panels A, B, C, D, and E present scatter plots reflecting the distribution of viral load:* ***(A)*** *HPV 16 genotype, distribution of NILM, ASC-US, and LSIL groups;* ***(B)*** *HPV 56 genotype, distribution of NILM, ASC-US, and LSIL groups;* ***(C)*** *HPV 58 genotype, distribution of ASC-US and ASC-H groups;* ***(D)*** *HPV 45 genotype, distribution of NILM and LSIL groups;* ***(E)*** *HPV 53 genotype, distribution of NILM and LSIL groups.*

Crucially, quantitative viral load possessed no direct linear relationship with the severity of cytological modifications. Peak viral loads were identified in women with normal cytology (NILM): HPV 31 (6.5 lg copies/10^5 cells), HPV 16 (7.3 lg copies/10^5 cells), and HPV 45 (5.89 lg copies/10^5 cells). Conversely, the single confirmed case of high-grade precancer (HSIL, associated with HPV 68 in a 44-year-old patient) was characterized by a relatively low level of viral DNA

(2.7 lg copies/10^5 cells). This indicates that during integration of the viral genome into host cell DNA in late stages, episomal replication decreases.

Combinations of multiple HPV genotypes were found in 20 women (21.5%). Quantitative strain profiles within co-infections are presented in Table 4.

Table 4. Quantitative strain profiles in mixed HPV infections

Genotype Combination	*TBS Status*	*Age (years)*	*Viral Load of Components Sequentially, lg copies/10^5 cells*
51/56	NILM	20	6.3 / 6.4
16/51	ASC-US	23	7.0 / 7.0
16/11	NILM	23	5.6 / 4.5
16/11	NILM	31	3.2 / 4.1
16/11	ASC-US	36	5.2 / 2.5
16/6	NILM	33	2.8 / 3.1
16/6	LSIL	20	7.0 / 4.2
16/58	NILM	35	6.5 / 4.0
16/68/51	ASC-US	24	6.5 / 6.6 / 6.0
11/66	NILM	39	1.69 / 1.41
16/51/39/66/59	ASC-US	32	4.8 / 4.4 / 4.5 / 4.2 / 6.5
16/56	NILM	41	1.4 / 3.2
16/56	LSIL	38	5.8 / 3.0
16/59	NILM	30	2.5 / 3.2
53/56	NILM	38	2.4 / 6.9
16/45/44	ASC-US	49	5.6 / 3.0 / 5.3
35/52	NILM	45	2.8 / 4.6
68/45/58/56	ASC-H	36	4.6 / 4.2 / 4.6 / 6.2
6/53	NILM	35	3.9 / 5.8
16/18/45	ASC-US	30	6.5 / 2.3 / 5.4
16/58/56	ASC-US	34	4.8 / 3.6 / 2.7

Note: *TBS - The Bethesda System**;** NILM - Negative for Intraepithelial Lesion or Malignancy; ASC-US - Atypical Squamous Cells of Undetermined Significance; ASC-H - Atypical Squamous Cells, cannot exclude HSIL; LSIL - Low-grade Squamous Intraepithelial Lesion**.** lg copies/10^5 cells d-ecimal logarithm of HPV DNA copies per 10^5 human cells. Viral load values are listed in the order of the corresponding genotypes separated by slashes (/).*

In mixed infections, two patterns were noted: uniform activity (e.g., 16/51 in ASC-US-both at 7.0 lg copies/10^5 cells; 51/56 in NILM-6.3 and 6.4 lg copies/10^5 cells) and a pronounced dominance of a single strain. A striking manifestation of inter-type competition was observed in the 53/56 combination: in a patient with NILM, type 56 dominated (6.9 lg copies/10^5 cells) versus 2.4 lg copies/10^5 cells; however, during the development of LSIL in another patient of the same age, dominance shifted to type 53 (5.8 lg copies/10^5 cells) versus 3.0 lg copies/10^5 cells. In the 5-component profile (16/51/39/66/59), the highest viral load was demonstrated by the relatively rare type 59 (6.5 lg copies/10^5 cells). More than half of the patients with mixed infections displayed normal cytological indices (55%), but in 45% of cases, pathological changes were recorded (ASC-US 30%, ASC-H 5%, LSIL 10%), suggesting a potential synergistic effect of combined genotypes on cell differentiation.

To evaluate the relationship between HPV genotype structure and overall cytological status, Pearson's χ^2 test was applied. A highly significant overall dependency was found between virus type and epithelial lesion character (χ^2=97.06; df=68; p=0.012).

Given the low frequencies in individual subgroups, Fisher's exact test was used to compute odds ratios (OR) for the risk of developing pathological cytology (ASC-US+ASC-H+LSIL+HSIL) relative to normal (NILM) (Table 5).

Table 5. Association of HPV genotypes with the presence of cervical cytological changes (n=93)

HPV Genotype	*Total Cases (n)*	*Odds Ratio (OR)*	*95% Confidence Interval (95% CI)*	*p-value (Fisher)*	*FDR-p (Benjamini-Hochberg)*
HPV 58	5	12.11	0.65-226.18	0.055	0.856
HPV 68	2	5.12	0.24-109.77	0.494	0.856
HPV 33	2	5.12	0.24-109.77	0.494	0.856
HPV 51	4	3.07	0.31-30.77	0.616	0.856
HPV 52	3	2.00	0.18-22.91	1.000	1.000
HPV 16	15	1.59	0.51-4.92	0.572	0.856
Mixed forms	20	0.75	0.27-2.04	0.618	0.856
HPV 56	8	0.56	0.12-2.49	0.484	0.856
HPV 45	5	0.23	0.02-2.12	0.202	0.856
HPV 53	5	0.23	0.02-2.12	0.202	0.856

Note: *n - number of cases; OR - odds ratio; 95% CI - 95% confidence interval; p-value (Fisher) - statistical significance calculated using Fisher's exact test; FDR-p (Benjamini-Hochberg) p-value adjusted for multiple comparisons using the Benjamini-Hochberg False Discovery - procedure. Statistical significance was set at* $p<0.05$.

The greatest pathological risk was demonstrated by HPV 58 (OR=12.11). This strain did not appear in a single case of normal cytology, inducing predominantly ASC-US (80%) and ASC-H (20%). Elevated risks were also discovered for HPV 68 and 33 (OR=5.12), as well as HPV 51 (OR=3.07). The probability of identifying abnormalities in carriers of the dominant HPV 16 was 1.59 times higher compared to others (OR=1.59; 95% CI 0.51-4.92). Due to the small sample volume for separate genotypes, the confidence intervals were wide, and after the Benjamini-Hochberg correction, statistical significance for isolated genotypes did not reach the critical level (FDR-p > 0.05), necessitating cohort expansion in future studies.

Discussion

The obtained findings characterize the genotypic and quantitative profile of HPV infection among women in the Samarkand region and display a combination of global patterns documented in the world literature alongside certain regional features. The most significant outcomes of the study include the predominance of HPV 16, the relatively low presence of HPV 18, a notable proportion of HPV 51, HPV 56, and HPV 58, the presence of multiple infections, and the lack of a direct relationship between viral load and the severity of cytological shifts. Combined, these data confirm the multifactorial nature of HPV persistence and cervical epithelial lesion formation. [47,48,49,50]

HPV 16 was the most frequently detected monoinfection (15 cases). Of these, 8 (53.3%) matched the NILM category, 2 (13.3%) matched ASC-US, and 5 (33.3%) matched LSIL. The

predominance of HPV 16 aligns with international research data, in which this genotype consistently occupies leading positions among high-risk oncogenic types and is uncovered in a large share of HPV-associated cervical cancer cases [1, 8, 12, 41, 51]. Concurrently, more than half of the HPV 16 cases identified in this study were accompanied by a normal cytological picture. This does not contradict the current understanding of the natural history of HPV infection, since finding viral DNA does not inherently equal the presence of neoplasia. A major portion of infections is transient and can be eliminated by the immune system, whereas the development of precancerous changes is more closely linked to infection persistence and long-term expression of viral oncoproteins E6/E7. Thus, the combination of high HPV 16 frequency with a predominance of NILM and LSIL may reflect different stages of the natural history of the infection-ranging from productive infection without morphological alterations to low-grade lesion development.

At the same time, the structure of other high-risk genotypes in the screened women possesses certain regional features. HPV 56 was detected in 8 cases, HPV 51 in 4, and HPV 58 in 5 cases. In international studies, HPV 16 and HPV 18 are traditionally treated as the primary oncogenic types; however, in Asian populations, HPV 58 and a series of other genotypes can carry substantially greater epidemiological significance [8, 12, 42, 43]. Therefore, the relatively notable presentation of HPV 51, HPV 56, and especially HPV 58 in the Samarkand region is of interest from a regional epidemiological standpoint.

HPV 58 warrants separate scrutiny. All five cases of its monoinfection were accompanied by pathological cytological results: four (80.0%) matched ASC-US and one (20.0%) matched ASC-H; no cases of NILM were registered among these patients. The observed trend is consistent with literature data pointing to the clinical weight of HPV 58 in forming cervical lesions, particularly in Asian populations. In the present study, relative risk calculation also yielded a high estimate of OR=12.11. However, interpreting this metric requires caution: the 95% CI was 0.65-226.18, and after adjusting for multiple comparisons, statistical significance was absent. Consequently, the obtained outcomes do not permit asserting that HPV 58 independently increases the risk of pathological cytology, but they do indicate a clear trend toward its association with cytological modifications. The limiting factor is the small number of observations; hence, a definitive assessment of the clinical value of this genotype requires evaluation in larger cohorts using histological verification.

In contrast, HPV 18 occurred much less frequently than HPV 16 in the investigated group: among monoinfections, only a single case was registered, which matched NILM. This differs from the epidemiological picture typical for many populations where HPV 18 holds second place after HPV 16. However, the low detection rate of HPV 18 in this sample does not signify a reduction in its biological oncogenicity, but rather reflects regional genotype distribution traits. Comparison with published data from Central Asian countries shows that the structure of separate high-risk types can indeed differ substantially between regions [24, 25, 26, 27, 52, 53].

Interesting observations were also obtained regarding HPV 68 and HPV 33. For HPV 68, two cases were registered-one LSIL and one HSIL, while HPV 33 was detected only with pathological cytological results matching ASC-US and LSIL. These findings are of definite interest considering the oncogenic potential of these genotypes; yet, the extremely small number of observations prevents making inferences about their individual risk. In particular, the single case of HSIL with HPV 68 cannot be viewed as proof of heightened oncogenicity for this genotype without validation in a larger cohort and, preferably, via histological methods.

Viral load demands separate consideration. The mean viral load in the evaluated group was 4.58±1.62 lg copies/10^5 cells. Simultaneously, a statistically significant link between age and viral load was not established: Pearson's correlation coefficient was r =-0.054 (p=0.578), and Spearman's ρ=-0.049 (p=0.612). More crucially, no simple linear dependency was observed between the amount of viral DNA and the severity of cytological changes. Thus, high viral load values were registered in certain women with NILM, including 7.3 lg copies/10^5 cells in HPV 16, whereas the sole case of HSIL in HPV 68 was characterized by a relatively low viral load-2.7 lg copies/10^5 cells.

The discovered pattern corresponds to contemporary models of HPV infection biology. The amount of viral DNA is not a direct equivalent of neoplasia grade, since the virus goes through a complex life cycle dependent on epithelial differentiation, the character of viral replication, and the host immune response [3]. A high viral load may reflect an active productive infection in the absence of pronounced cytological changes. On the contrary, with lesion progression, a shift in the ratio of episomal and integrated forms of viral DNA is possible, which can potentially be accompanied by a decrease in the volume of freely replicating viral genome. However, because HPV integration was not directly measured in the current study, this explanation should be viewed as a biologically grounded hypothesis rather than a proven mechanism. Therefore, viral load in the studied population may be treated as an additional characteristic of HPV infection, but not as an independent marker of cytological lesion grade.

Another significant finding is the identification of multiple HPV infections in 20 out of 93 women, accounting for 21.5%. This frequency lies within the range described for other populations, though in separate Central Asian studies, the rate of mixed infections can be higher. In our sample, 55.0% of mixed infections matched NILM, 30.0% matched ASC-US, 5.0% matched ASC-H, and 10.0% matched LSIL; no HSIL cases were uncovered among multiple infections. Consequently, multiple infections themselves did not exhibit an obvious link with more severe cytological injury. Viral load differences between components of a single mixed infection also indicate unequal quantitative representation of individual genotypes. For example, in the HPV 53/56 combination, the viral load was 2.4 and 6.9 lg copies/10^5 cells, respectively, and in the HPV 16/51/39/66/59 combination, it was 4.8, 4.4, 4.5, 4.2, and 6.5 lgcopies/10^5 cells. However, these differences cannot be directly interpreted as proof of genotype competition, because confirming such interrelations requires longitudinal studies with serial monitoring of each HPV type.

The overall structure of cytological findings further accentuates the multifactorial nature of HPV-associated injury. Among 93 women, NILM was revealed in 46 (49.5%), ASC-US in 23 (24.7%), LSIL in 20 (21.5%), ASC-H in 3 (3.2%), and HSIL in 1 (1.1%). Thus, nearly half of the HPV-positive women had no cytological markers of a lesion. This aligns with modern models of the natural history of HPV infection, according to which most infections are transient, while precancerous development is linked primarily to infection persistence and the interaction of viral factors with host organism traits [1, 6, 44].

It is probable that differences in infection outcomes are driven not only by viral genotype and its DNA quantity but also by a constellation of host factors. Modern studies highlight the value of the immune response, epigenetic mechanisms, microRNAs, chromosomal instability, and other cellular homeostasis regulation mechanisms in the transition from infection to a neoplastic process. The state of the cervical microbiota may provide additional significance [4, 5, 9, 45]. The dominance of *Lactobacillus* spp. is associated with a more favorable local environment, whereas dysbiotic shifts can facilitate HPV persistence and cervical lesion development [15, 16]. Since the

microbiome was not evaluated in this study, its role in the discovered patterns remains speculative and constitutes a prospective direction for future investigations.

From a practical angle, the identified genotypic profile carries weight for prevention. The 9-valent vaccine provides protection against HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58. Several genotypes contained within this vaccine were represented in the study sample, including HPV 16, 18, 33, 52, and 58. This underscores the potential preventive value of expanded vaccine coverage. Simultaneously, the notable presence of HPV 51 and HPV 56, which are not included in the 9-valent vaccine, confirms the necessity of preserving organized screening even under conditions of expanded vaccination coverage. Vaccination and screening must be viewed as complementary components of prevention, since no existing vaccine covers the full spectrum of oncogenic HPV types [6, 17, 18, 46].

Thus, the completed study demonstrates that the epidemiological profile of HPV infection in the Samarkand region overall matches global trends, but simultaneously features regional characteristics. HPV 16 maintains its dominant position; however, nearly half of the HPV-positive women present with a normal cytological picture, highlighting the need to distinguish between the fact of infection and a clinically significant persistent lesion. Concurrently, the high representation of HPV 51, HPV 56, and HPV 58 points to a more complex regional genotypic spectrum than the classical model of HPV 16/18 dominance. The identified trend toward an association of HPV 58 with pathological cytological results is especially interesting, though due to the small number of observations and wide confidence interval, it demands confirmation.

To clarify the prognostic role of individual genotypes, primarily HPV 58, larger prospective studies are needed, utilizing dynamic observation, serial genotyping, and viral load measurements, alongside expanded colposcopy and histological verification of identified lesions. This approach will help determine which genotypes are linked not just to the presence of HPV infection, but to its persistence and subsequent progression into cervical neoplasia.

Conclusion

The performed study enabled characterization of the genotypic and quantitative profile of HPV infection among women in the Samarkand region and established the traits of its relationship with the cervical cytological state. The predominance of HPV 16 among monoinfections was established alongside a relatively low rate of HPV 18, as well as a notable presence of HPV 51, HPV 56, and HPV 58, indicating regional variations in the high-risk oncogenic HPV genotype spectrum.

Nearly half of the screened HPV-positive women presented with a normal cytological picture (NILM), confirming the lack of direct alignment between the fact of detecting viral DNA and the presence of cytological changes. The most pronounced trend toward an association with pathological cytological results was noted for HPV 58: all identified cases of its monoinfection were accompanied by changes in the cytological picture. However, wide confidence intervals and the absence of statistical significance after adjustment for multiple comparisons prevent treating HPV 58 as an independent predictor of injury and demand validation in larger cohorts.

The mean viral load was 4.58±1.62 lg copies/10^5 cells. No statistically significant link was found between viral load and age, nor was an unambiguous dependency on cytological lesion grade established. Uncovering a high viral load in NILM and a relatively low load in HSIL indicates that the quantitative content of viral DNA cannot be treated as an independent index of cervical lesion severity.

Multiple HPV infections were identified in 21.5% of the evaluated women. Most mixed infection cases were not accompanied by severe cytological alterations, which does not confirm its direct link with more severe cervical injury. Thus, the character of cytological changes is determined by a combination of viral and host factors, including genotype specifics, infection persistence, and the state of local and systemic immune responses. The obtained findings carry practical value for improving regional prevention of HPV-associated diseases. Identifying genotypes contained within the 9-valent vaccine confirms the potential value of expanded vaccination, while the circulation of HPV 51 and HPV 56, which are not included in it, underscores the necessity of retaining effective cytological and HPV screening.

In general, the study findings confirm that cervical lesion risk assessment must be grounded in a comprehensive characterization of the HPV infection, accounting for viral genotype, cytological status, and persistence dynamics, rather than on a single viral load indicator. A promising direction for future research involves the prospective follow-up of HPV-positive women with serial genotyping, quantitative viral load assessment, colposcopy, and histological verification, which will clarify the prognostic meaning of individual genotypes, primarily HPV 58, in the development and progression of cervical neoplasia.

Study Limitations

A limitation of this study is the lack of histological data (biopsy) and expanded colposcopy, which prevented final verification of intraepithelial neoplasia grades and more precise matching of morphological changes with identified HPV genotypes. Furthermore, incomplete recording of patient somatic and obstetric-gynecological histories limited the ability to comprehensively evaluate long-term risk factors for HPV persistence and cervical lesion development. An additional limitation was the absence of laboratory evaluation for concurrent immunodeficiency states, which can impact HPV clearance or persistence and, consequently, the probability of dysplastic change progression. These limitations should be factored in when interpreting the obtained findings and planning future research.

Abbreviations

AGC	Atypical glandular cells
ASC-H	Atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion
ASC-US	Atypical squamous cells of undetermined significance
CI	Confidence interval
CST	Community state types
df	Degrees of freedom
DNA	Deoxyribonucleic acid
FDR	False discovery rate
HCG	Hyperchromatic crowded cell groups
HPV	Human papillomavirus
HPV	HR High-risk human papillomavirus
HSIL	High-grade squamous intraepithelial lesion
IQR	Interquartile range
LBC	Liquid-based cytology
lg copies/10^5	cells Decimal logarithm of viral DNA copies per 10^5 host cells
LLC	Limited liability company
LSIL	Low-grade squamous intraepithelial lesion
M	Mean

Me	Median
NILM	Negative for intraepithelial lesion or malignancy
OR	Odds ratio
p-value	Probability value
PCR	Polymerase chain reaction
RNA	Ribonucleic acid
SD	Standard deviation
SRC	Sample received control
TBS	The Bethesda system
VL	Viral load
χ^2	Chi-squared Pearson's criterion

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Authors' Contributions

G.Kh. Yarmukhamedova and S.V. Kan developed the concept and design of the study. S.V. Kan and G.A. Dushanova conducted the literature search and data collection. G.Kh. Yarmukhamedova, G.Z. Ziyadullaeva, and S.A. Khalilova performed statistical data analysis and drafted the manuscript. S.V. Kan, G.A. Dushanova, and M.K. Yarmukhamedova provided critical reviews and edited the manuscript. M.K. Yarmukhamedova served as an external consultant on HPV infection. All authors critically reviewed, read, and approved the final version of the manuscript.

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Data Availability

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

Declarations:

Ethical Approval and Consent to Participate: The study was conducted in accordance with the principles of the Declaration of Helsinki. The study protocol was approved by the Local Bioethics Committee of Samarkand State University named after Sharof Rashidov (Protocol No. 8, 2026). Informed consent was obtained from all participants or their legal representatives.

Consent for Publication: Not applicable.

Conflict of Interest: The authors declare no conflict of interest.

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