



Examination of the prevalence of high-risk human papillomavirus genotypes among women on the territory of Belgrade

Ispitivanje zastupljenosti visokorizičnih genotipova humanog papiloma virusa kod žena na teritoriji Beograda

To the Editor:

Cervical cancer is the fourth most common malignant tumor after breast cancer, colorectal cancer, and lung cancer, which threatens the health of women worldwide¹. Persistent infections by specific high-risk (HR) human papillomavirus (HPV) – HR-HPV strains are the leading cause of cervical cancer and precancerous lesions².

HPV infection has the highest transmission rate among sexually transmitted diseases caused by viral agents³. HPV is an etiological factor in the development of malignant lesions of the anogenital tract, cervix, vagina, vulva, and penis, as well as the head and neck region, that is, the pharynx, larynx, mouth, esophagus, and respiratory tract⁴. Most HPV infections are self-limiting and remain at the individual level for 15–18 months until the immune system develops a defensive response to the presence of the pathogen. The infection caused by HPV is most often asymptomatic⁵.

Based on a direct causal link between HPV infection and cancer development, the American Society for Colposcopy and Cervical Pathology guidelines, World Health Organization, European Society Gynecological Oncology, and European Federation of Colposcopy, suggest HPV deoxyribonucleic acid (DNA) testing as the primary method of HPV detection^{6–8}.

The advantage of this method is the high sensitivity of polymerase chain reaction (PCR) molecular tests, which ensure the identification of different HPV types, primarily HR-HPV 16 and HR-HPV 18, with a small number of false negative results, which can, with high reliability, declare a low risk for the development of cervical intraepithelial neoplasia 3 (CIN 3) lesions in persons with a negative HPV result⁹. Approximately 52% of CIN 3 lesions are associated with HPV 16 and 18 and represent HR lesions corresponding to precancerous disease¹⁰.

Based on the report of the International HPV Reference Center, there are more than 200 different genotypes of HPVs¹¹. HPV genotypes are classified based on the potential to cause the development of malignancy into HR-HPV and low-risk (LR) HPV – LR-HPV types¹². Of this number of different genotypes, only 50 can induce infection of the cervical epithelium. However, only 14 HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68) were classified as HR types¹².

The presented study aims to assess the prevalence of HR-HPV genotypes among women who have undergone regular gynecological examinations in the territory of Belgrade, Serbia. The study included the analysis of 847 clinical samples, collected from May to October 2023, aged 19 to 60 years. The samples were collected and analyzed at the Institute of Public Health of Serbia “Dr. Milan Jovanović Batut”. Viral DNA extraction was performed on a KingFisher Duo Prime (Thermo Fisher Scientific, Inc.) using the RealLine DNA – Extraction 3 magnetic extraction kit (Bioron diagnostics)^{13, 14}. The applied test for DNA detection of 14 HR-HPV genotypes (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68) was Viasure High-Risk Human Papilloma Virus diagnostic test (CerTest Biotec, S.L.)¹⁵. By analyzing collected samples, 271 (32%) were positive, while the remaining 570 (68%) were negative for any HPV genotype.

Among the positive samples, only one HPV genotype (HPV 16 or HPV 18 or one of the groups of HR-HPV genotypes) was detected in some of the samples, and, in the rest of the samples, more than one HR-HPV genotype, i.e., co-infection, were detected. Within the positive samples, the genotype HPV 16 was detected in 74 (27%) samples regarding single infection and co-infection. The genotype HPV 18 was detected in 31 samples regarding single infection and co-infection and showed a frequency of 11%. The HPV group (31, 39, 56) showed the highest rate of detections, 126 (47%)

samples when it comes to single-type infections and co-infections by other HPV groups and HPV 16 and 18.

Based on the presented results, the highest prevalence was shown by the genotype of the HPV group (31, 39, 56), followed by HPV genotype 16, in all the positive samples. The presented results also indicate that a very high percentage of women who have undergone regular gynecological examinations on the territory of Belgrade are infected with some of the HR-HPV genotypes. The positive results according to detected HPV genotypes are equally distributed among all of the age-related groups of women analyzed in this study. Thirty-two percent of randomly selected women is a relatively worrying figure. The high prevalence of HR-HPV genotypes represents an indicator of recognition of the need for a wider area of education and prevention of the general population of women.

HPV genotyping promises the potential to refine the algorithm for the management of HR-HPV-positive women after treatment. Risk stratification allows suitable recommendations for colposcopies and treatments to women with the highest risk of cervical diseases, while women with the lowest risk of pathological changes should be re-examined at short intervals. This would utilize healthcare resources more effectively and reduce patients' psychological anxiety.

**Hristina Gospodinović*, Edita Grego*,
Sofija Jovanović†, Ljiljana Pavlović***

***Institute of Public Health of Serbia "Dr. Milan Jovanović Batut", Belgrade, Serbia; †University of Belgrade, Faculty of Medicine, Belgrade, Serbia**

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