Introduction

Human papilloma virus is a small virus of 55 nm diameter and comprises a double-stranded circular DNA of nearly 8000 base pairs. The coat of the virus contains two proteins, one major L1 and one minor, L2. Regarding the L1 protein, this can be identified 100 different genotypes. The HPV genome encodes eight proteins: early proteins (E5,E6,E7) involved in cell proliferation and E6 and E7 play a key role in carcinogenesis by inactivating p53 oncogene. (1,2) The link between cervical cancer and HPV was recognized by Harald zur Hausen, who received the Nobel Prize in 2008 (3).

In gynaecological pathology, HPV is implicated in cervix cancer (> 95%), vaginal cancer, vulvar cancer, anal cancer and penile cancer. In carcinogenesis 3 groups of HPV are involved: high risk (HR), low risk (LR) and unknown risk (UR). The most frequent types associated in more than 70% of cervix cancer and 50% of high squamous intraepithelial lesions (HSIL) are 16 and 18 types (4). Also, this virus is present in head & neck cancer with 6 and 15 types (5).

Patients and methods

In this prospective study between January 2010 and August 2014 192 cases were included: 115 cases of carcinoma, 62 cases with dysplasia and 15 cases with pelvic inflammation. The HPV samples were taken by two gynaecologists, who treated the dysplasia and pelvic inflammation cases.

All malignant cases were treated and followed in our Clinic of Oncology and Radiotherapy Department, Oradea. Each of the patients required: biopsy, oncological...
study of HPV in cervix pathology, and was evaluated for follow up according to the Oncological Guidelines.

The DNA isolation and the HPV detection and genotyping was performed at the Residence Laboratory Oradea with PCR technique. The HPV positive samples were genotyped by Restriction Fragment Length Polymorphism (RFLP) method (PGMY positive samples) or by DNA sequencing (GP5+/GP6+ positive samples).

HPV types detected by the RFLP method are as following:

- High-risk: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, 82;
- Undetermined – risk: 26, 53, 66
- Low-risk: 6, 11, 13, 30, 34, 40, 42, 43, 44, 54, 55, 61, 62, 64, 67, 69, 70, 72, 74, 81, 83, 84

HPV types detected by DNA sequencing: virtually all types. HPV detection sensitivity: 1-10 HPV genomes in the background of 100 ng of human DNA.

Results

In all 115 cases of carcinoma, HPV determined was positive in 60 patients (52.17%).

As for age repartition, HPV + was found: under 30 years, 4 patients (100%), between 31-40 years group (61.54%), between 31-40 years group (61.54%).

Stage III FIGO was the mostly affected by HPV + (55%), followed by stage II FIGO (26.67%).

Based on HPV case distribution, the majority had only one HR type (75.61%), 16 HR was 56.10%, 18 HR was 7.31% and 45HR was 4.88%. The most frequent associations of HR types were between 16 + 33 HR (12.2%), followed by 16 + 31 HR (4.88%) and 31 + 33 HR (4.88%).

From LR type, 4 patients, were discovered with 1 case of 61LR, 62LR, 70LR, 83LR.

From 5 cases HPV – UD we found 3 cases with 53UD and 2 cases with 66UD.

Figure 2. HPV + stage distribution HPV prevalence showed that more than 35.65% were HR, followed by associations (8.7%) , LR and UD were under 5%.

Among 10 cases of HPV associations HPV-HR was revealed in all patients , 16 HR in 6 cases.

Disease free survival over 3 years was found in 18.18 % patients with HPV-HR, in 33.33 % patients with HPV-LR, in 20.00% patients with HPV-UD and in none of the associations.

Figure 3. HPV types

Figure 4. DFS and HPV
From the total of 16 deaths, 12 were identified with HPV+, with a mortality of 20.00% of the total HPV+ patients. The mortality in HPV- patients was 7.2%, statistically significant (p<0.001).

**Discussion**

In our study we had a high incidence of HPV cases, especially in young patients and unfortunately in advanced stages of disease. A multivariate analysis of HPV+ types and age shows that HPV-HR was the only type found in all age groups. In under 30 year patients, all HPV+ cases were with HPV-HR, at 31-40 years group 75% of HPV+ cases were HR type and 25% were UD, at 41-50 years group and over 60 years we found all HPV types, including associations.

In our results the most implicated HPV+ HR type was 16, as mentioned in literature data (6).

International studies have shown a great interest in the prognostic value of HPV genotypes in cervical cancer treated with concurrent radiochemotherapy, such as Wang’s studies for advanced squamous cervix carcinoma (7,8). Also, the clinical implications of HPV genotypes in adeno-squamous carcinoma have been studied, revealing as negative prognosis factors: age > 50 years, HPV16 + and FIGO stage III - IV (9).

The presence of HPV 18 genotype appeared as a poor prognostic factor in women with early disease, as Gadducci et al observed (10).

**Conclusions**

As our study revealed, it would be useful to determine HPV in all cervix cancer patients, at least HR types. Their presence can be considered a negative prognosis factor in the treatment response, disease free survival and overall survival.

**References**


**Author’s disclosures of potential conflicts of interest.** The authors indicated no potential conflicts of interest.