

## THE PREVALENCE OF HIGH RISK HPV STRAINS IN HIV POSITIVE PATIENTS – A PRELIMINARY STUDY

SORIN ANDREI<sup>1</sup>, ANDREIA PAULA RÎMBEȚ<sup>2</sup>, LUCIAN PUȘCAȘIU<sup>3</sup>, KLARA BRÂNZANIUC<sup>4</sup>

<sup>1,2,3,4</sup>University of Medicine and Pharmacy Tîrgu-Mureș

**Keywords:** HPV infections, high risk prevalence, HIV positive patients

**Abstract:** At the end of the 80s, Romania has faced one of the saddest public health problems: children infected with HIV as a result of medical procedures performed in hospitals. This situation has not been disclosed before 1989, and as a result the first cases of HIV infections in children in Romania have been identified this year. The aim of our study is to study the presence of the human papilloma virus infection, and analyze the prevalence of highly oncogenic HPV strains in this special group of patients. The samples were processed at a genetics laboratory for molecular testing. The molecular genetic testing enables high sensitivity detection of HPV infection and genotyping of different strains: of high risk, of undetermined risk and of low risk. From the total of 37 HIV positive patients between 20 and 24 years old, who became HIV infected parenterally during childhood, the results were abnormal in 16 cases, and in the rest of 21 cases, the results were negative. HPV genotyping revealed high risk strains in 8 cases (59 in 5 cases, and 31 in 3 cases), undetermined risk strains in 4 cases (53 in all cases), and low risk strains in the remaining 4 cases (11 in 3 cases and 4 in one case). The inclusion of HPV testing in cervical cancer screening of patients with iatrogenic HIV infection acquired during childhood needs further evaluation and validation. The potential benefit would be an increase in the detection rate, lengthening the testing intervals, decreasing the number of visits and unnecessary medical procedures, and the correct treatment of the detected lesions.

**Cuvinte cheie:** tulpini HPV, risc înalt, prevalență, pacienți HIV pozitivi

**Rezumat:** România la sfârșitul anilor '80 a fost pusă față în față cu una din cele mai dureroase probleme de sănătate publică: copiii infectați cu virusul HIV în urma unor proceduri medicale, ce au avut loc în spitale. Această situație nu a fost făcută publică mai devreme de 1989, astfel încât primele cazuri de infecție HIV la copil în România au fost identificate în acest an. Obiectivul studiului nostru este de a cerceta prezența infecției cu Virusul Papiloma Uman și de a analiza prevalența tulpinilor HPV înalt oncogene la acest grup special de pacienți. Testul molecular genetic permite la un nivel mare de sensibilitate detecția infecției HPV și genotiparea mai multor tipuri de tulpini: de risc mare, de risc nedeterminat și de risc scăzut. Din totalul celor 37 de pacienți HIV pozitivi cu vârsta cuprinsă între 20 și 24 de ani care au contactat infecția HIV pe cale parenterală în copilărie rezultatele au fost anormale în 16 cazuri, în restul de 21 de cazuri rezultatul fiind negativ. Tipajul HPV a decelat tulpini cu risc mare în 8 cazuri (59 în 5 cazuri, respectiv 31 în 3 cazuri), risc nedeterminat în 4 cazuri (de fiecare dată 53), respectiv risc scăzut în restul de 4 cazuri (11 în 3 cazuri și 4 un caz). Incluziunea testării HPV în screening-ul cancerului de col uterin la pacienții HIV pozitivi cu infecția dobândită iatrogen în copilărie necesită evaluări și validări ulterioare acestui studiu preliminar. Potențialul beneficiu ar fi creșterea ratei de detecție, lungirea intervalelor de testare, reducerea vizitelor și actelor medicale inutile și tratamentul adecvat al leziunilor decelate.

### INTRODUCTION

At the end of the 80s, Romania has faced one of the saddest public health problems: children infected with HIV as a result of medical procedures performed in hospitals. This situation has not been disclosed before 1989, and as a result the first cases of HIV infections in children in Romania have been identified this year.(1)

In case of HIV positive patients, the main genital pathologies are invasive cervical cancer and its precursor lesions (2,3), as HIV infection is a high risk condition for developing HPV infection.(4) Additionally, oncogenic HPV strains represent the most important etiologic factor of cervical cancer.(5) On the other hand, Romania has the highest rate of mortality from cervical cancer in Europe (13/100 000), i.e. a 6.3 fold higher rate than in other European countries.(6,7)

### PURPOSE

The aim of our study is to study the presence of the human papilloma virus infection, and analyze the prevalence of highly oncogenic HPV strains in this special group of patients.

### METHODS

The study has been conducted at the 1st Obstetrics and Gynecology Clinic from Tîrgu-Mureș, after favourable authorization has been obtained from the Ethics Committee of the University of Medicine and Pharmacy, Tîrgu-Mureș. All patients have been correctly informed about the study, and signed an informed consent document.

Of the total of 148 HIV positive women registered in the records of the from Tîrgu-Mureș Regional Centre from the 1st Infectious Diseases Clinic, we decided to include in the

<sup>1</sup>Corresponding author: Sorin Andrei, Str. Ghe. Marinescu, Nr. 50, Tîrgu-Mureș, România, E-mail: andreisorin9@gmail.com, Tel: +40744 84346  
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study only the patients aged from 20 to 24 years old, as all of them became HIV infected during childhood, as a result of medical procedures performed at hospitals.

A total of 37 patients remained, and in their case an endocervical secretion sample has been taken through brushing, using a rotating plastic brush, according to the manufacturer's instructions. The samples were used for HPV genotyping. The samples were processed at a genetics laboratory for molecular testing. The molecular genetic testing enables high sensitivity detection of HPV infection and genotyping of different strains: of high risk: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, 82; of undetermined risk: 26, 53, 66; of low risk: 6, 11, 13, 30, 34, 40, 42, 43, 44, 54, 55, 61, 62, 64, 67, 69, 70, 72, 74, 81, 83, 84, 91.

Molecular testing is based on amplifying a DNA sequence present in all HPV strains using PCR. The amplified sequence contains certain differences specific to different strains, and detection of these differences enables precise genotyping of the existing strain/strains. In order to obtain high sensitivity and specificity the molecular testing uses two sets of PCR primers and internal quality control, thus excluding false negative results.

### RESULTS

From the total of 37 HIV positive patients between 20 and 24 years, who became HIV infected parenterally during childhood, the results were abnormal in 16 cases, and the rest of 21 cases the results were negative. HPV genotyping revealed high risk strains in 8 cases (59 in 5 cases, and 31 in 3 cases), undetermined risk strains in 4 cases (53 in all cases), and low risk strains in the remaining 4 cases (11 in 3 cases and 4 in one case).

### DISCUSSIONS

Beginning from the year 1993, the Centres for Disease Control and Prevention (CDC) from the USA included cervical cancer on the list of conditions defining AIDS.(8)

Additionally, there is a general consensus regarding persisting high risk HPV infection as a necessary factor for the development of cervical cancer and precancerous lesions – grade 3 cervical intraepithelial neoplasia. Epidemiologic studies have demonstrated that almost 100% of the cervical cancer cases were positive for HPV.(9)

The HPV 16 strain is the most carcinogenic genotype and it is associated with approximately 55 – 60% of the cervical cancer cases.(5,9,10) The next strain with carcinogenic impact is HPV 18, occurring in about 10-15% of cervical cancers. It is associated especially with glandular cancers (adenocarcinoma and adenosquamous carcinoma), and not with squamous cell cancer, in a ratio of 32%, and 8%, respectively.(5,9,10)

Establishment of the causal relationship between HPV infection and cervical cancer, in conjunction with epidemiologic data and natural history of HPV infection, has generated the current model for cervical cancer carcinogenesis, as the following sequence: HPV infection, persisting HPV infection (as opposed to neutralization), progression to cervical dysplasia and eventually invasion.(11,12)

Genital HPV infection occurs via sexual transmission or by skin contact with the genital area, and the prevalence is maximal at around a few years after the initiation of sexual activities.(13)

An overwhelming majority (90%) of HPV infections become undetectable after 1-2 years.(14,15)

In case of women with persisting infection, the risk of developing precancerous lesions is significantly increased. Therefore, persistence of HPV16 for 1-2 years is a good

predicting factor for the development of CIN3 in the subsequent years.(16,17,18,19)

In case of no treatment, CIN3 has a 30% probability of progression to invasive cancer in the next 30 years, while once treated, only 1% of the CIN3 cases will progress to invasive cervical cancer.(20)

The fundamental role of cervical cancer screening is to reduce cervical cancer morbidity and mortality. This screening has to be offered and tailored to patients in certain risk groups, like HIV positive patients, despite the results of some preliminary studies that did not confirm an increased incidence of dysplasias in these patients.(3,21) HPV testing seems to better predict which patients will develop CIN3 in the next 5 to 15 years, than cytology alone.(22-24)

### CONCLUSIONS

Inclusion of HPV testing in cervical cancer screening of patients with iatrogenic HIV infection acquired during childhood, needs further evaluation and validation.

The potential benefit would be an increase in the detection rate, lengthening the testing intervals, decreasing the number of visits and unnecessary medical procedures, and the correct treatment of the detected lesions.

During elaboration of practical guidelines, we should mandatorily account for the epidemiologic characteristics of these HIV positive patients infected during childhood, with early diagnosis and inclusion into national programmes for treatment and monitoring, with good compliance to treatment and satisfactory immunological status. However, by now, these women reached the reproductive phase of their lives, with all the epidemiological consequences.

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