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Epidemiological Characteristics of the Human Papilloma Virus in Women in Uzbekistan

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Abstract—*This article examines the epidemiological characteristics of the human papillomavirus in Uzbekistan. The report presents data on the prevalence of phylogenetic groups identified as a result of the research carried out, as well as the age-specific features of the spread of the human papillomavirus and their combination. Recommendations on preventing the spread of human papillomavirus by introducing vaccination and conducting screening tests for women to prevent cervical cancer.*

Keywords—*human papillomavirus, phylogenetic groups, cervical cancer, screening, vaccination.*

I. INTRODUCTION

Human papillomavirus (HPV) is a widespread virus that causes a variety of diseases in both women and men. About 400 different types of human papillomavirus are now known, of which 80 types are the most studied, and about 15 types cause lesions of the female genitalia. The most dangerous of these are the types of HPV with high carcinogenic risk, the viruses with the greatest ability to cause genital cancer, in particular, cervical cancer. The most dangerous are those: 16, 18, 31, 33, 35, 39, 45, 51 and 52 types of HPV. The most important manifestations of HPV in women are acute and flat conditioners, dysplasia (precancer) and cervical cancer. It is time to study more closely the epidemiological characteristics of HPV, with a high risk of developing oncological cellular degeneration due to exposure to the virus, into a serious disease such as cervical cancer (CC). [3, 4, 12]. There is an urgent need for activities aimed at preventing CC. This issue has to be solved on a global scale; a special place in the solution of the CC problem is the early diagnosis of precancerous conditions and, most importantly, vaccination. [10]. Currently, there is a modern system of early diagnosis of HPV, laboratory technologies have advanced significantly, there is a method of polymerase chain reaction (PCR), and this method in its modern form can already quickly detect entire viral genomes and sequencing the genome of the HPV host [6, 7, 8]. Today, there are various methods of HPV diagnostics, but this does not solve the problem of RSHM, and this problem remains a serious burden worldwide. We need to focus our efforts on primary prevention, in which case vaccination is the most effective method of prevention.

The aim of the study. To study the epidemiological peculiarities of HPV among women to determine the strategy for prevention of CC (cervical cancer) in the Republic of Uzbekistan.

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II. MATERIALS AND METHODS

Materials: Women who have undergone examinations at the National Specialized Scientific and Practical Medical Centre for Obstetrics and Gynecology. A total of 6,431 women were screened between 2015 and 2018 to determine the phylogenetic group of HPVs. The study includes the results of the testing of women aged 18 to 65 years.

Methods: The determination of the phylogenetic group of HPV and the viral load of women seeking diagnostic services was based on a study of cytological material from the cervical canal scrape. Testing was performed with the help of the "Amplicence® HPV of HPV of HCR screen-title FRT" test system in the "real-time" mode, which allows to differentiate 12 HPV genotypes of high carcinogenic risk in the "multiplex" format. The set of "HPV Amplicence® HPV screen-titer FRT" reagents can detect HPV DNA of three main phylogenetic groups - A7 (18, 39, 45, 59 types) and A9 (16, 31, 33, 35, 52, 58 types), as well as A5/A6 (51 and 56 types) types. The detection of the 12 most common types of human papillomavirus at high carcinogenic risk by this set of reagents is sufficient to achieve high diagnostic sensitivity of the test. Statistical processing of the results is carried out using the statistical applications SPSS 16, 21 and STATA 10.0 SE. Descriptive statistics are used to calculate 95% of the confidence intervals and to simulate the economic model with sensitivity analysis. In order to determine the dependence of the age indicator of the examined patients on phylogenetic, age and virus concentration groups, the average age indicator for positive and negative patients was compared for the presence of each phylogenetic group separately using the T-criterion for independent samples.

III. RESULTS

Between 2015 and 2018, a survey of 6,431 women was conducted to determine the phylogenetic group of the HPV. Approximately 2,000 women were surveyed each year, and the low number of women surveyed in 2015 was due to the fact that diagnostic services were only available during the last quarter of the year.

The study included test results for women aged 18 to 65 years. In order to analyze the data, we have divided all women into 8 age groups: 18-24; 25-29; 30-34; 35-39; 40-44; 45-49; 50-54; over 55 years of age. The total number of tests carried out was 6431, of which 1162 (18.1%) were positive. The highest incidence of HPV was registered at the age of 22 to 35 years, with a gradual decrease in the indicators. The highest rate of HPV was registered at the age of 31 - 38.5%, and then at the age of 33 - 36%. Under 22 years of age, HPV infection rates are lowest. HPV is present at all ages above 40 years of age, but the incidence is significantly lower than under 40 years of age, ranging from 1 to 10 per cent.

The age distribution compensates for the impact of variations in detection rates at individual ages, which provides an average picture of HPV prevalence in Uzbekistan (Figure 1). Thus, the prevalence among age groups repeats HPV epidemiology on a global scale, when, starting with the age of sexual activity of women, the risk of HPV infection increases, the level of HPV detection increases, reaches its maximum at the age of 25-35 years, and then there is a decrease in the detectability of this indicator.

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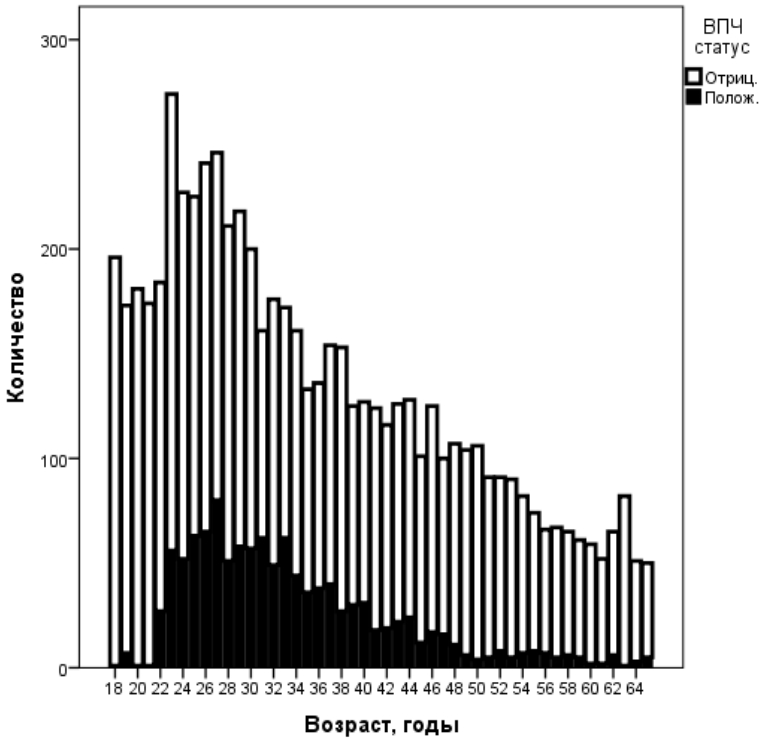
Figure 1. Dynamics of absolute HPV detection rate by age of patients



Thus, in the age group 18-24 years the prevalence of HPV infection was 10.3±0.8%, in the age groups 25-29 years, 30-34 years and 35-39 years the highest levels of 27.8±1.3%, 31.5±1.6% and 24.4±1.6%, respectively, with the indicators in these age groups at the level of $p<0.001$ spastically higher than in other age groups. With increasing age, the indicators decrease, so in age groups: The index of 45-49 years is equal to 11.5±1.4%, 50-54 years - 6.3±1.1%, older than 55 years - 7.2±1.0%, in these age groups the indexes are statistically significantly lower than in the previous age groups at the level of $p<0.001$. the results obtained in our study confirm the data of the Russian authors [1]. It is known that HPV is one of the markers of women's sexual activity, so our data is a confirmation of this. The peak of HPV detection in the age group under 18-35 years old. After 35 years of age, viruses are diagnosed less frequently and there is a gradual decrease in detectability (Table 1).

Table 1 Incidence of HPV infection in different age groups

Age group	Number of examined	Number of positive	Mean(M ± m)	Significance of Differences
18-24 years	1409	145	10,3±0,8	a
25-29 years	1141	317	27,8±1,3	b
30-34 years	870	274	31,5±1,6	b
35-39 years	701	171	24,4±1,6	b
40-44 years	621	114	18,4±1,6	c
45-49 years	537	62	11,5±1,4	d
50-54 years	460	29	6,3±1,1	d
Older 55 years	692	50	7,2±1,0	d
Всего	6431	1162	18,1±0,5	

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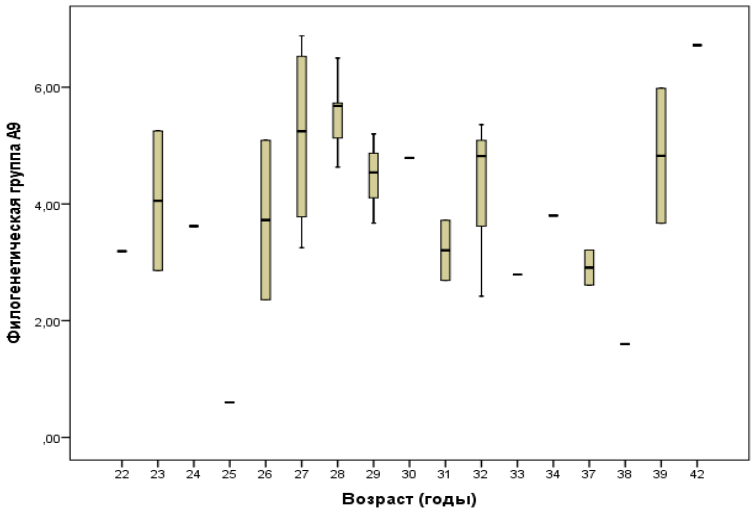
Note: a - the age group index at the level of p<0.001 differs from the age groups of 25-44 years; b - the age group index at the level of p<0.001 differs from the age groups of 18-24 years and 40 years and older; c - the age group index at the level of p<0.001 differs from the age groups of 18-34 years and 50 years and older; d - the age group index at the level of p<0.001 differs from the age groups of 24-44 years.

To estimate the prevalence of different phylogenetic groups, 1184 studies were conducted. Evaluation of the frequency of occurrence of phylogenetic groups yielded the following results: the most frequent types were A5/A6 (51 and 56 types) in 631 (54.2±1.4) cases, A7 in 508 (18, 39, 45, 59 types) (43.6±1.4) cases, A9 (16, 31, 33, 35, 52, 58) in 331 (28.4±1.3) cases, with statistically significant differences (p<0.001).

As a result of the analysis, the following results were obtained: the average age of patients who applied to medical institutions to determine HPV in all phylogenetic groups was 31-32 years. The mean age indicator for the phylogenetic group A9 was 31.4±0.4 years, for the phylogenetic group A7 the mean age was 32.3±0.3 years, for the group A5/A6 this indicator was 32.1±0.3%. At the same time, the indicators did not have a statistically significant difference between the groups.

The age distribution of each phylogenetic group repeats the general picture of the distribution of HPV detection, with an increase in the age of up to 20 years, the maximum level at the age of up to 30 years and a gradual decrease in the aftermath. At the same time, there are no significant differences in the age distribution, apart from the general level, between the groups.



Picture 2. Distribution of HPV concentration (lg HPV per 100 thousand cells) of infection of phylogenetic group A9 depending on age.

Note: The graph is a median distribution of the indicator - arithmetic mean (middle of the rectangle), 25% and 75% quartile (upper and lower bounds of the rectangle), and 95% range (t-band). Samples presented in single digits are displayed as a dash.

In the phylogenetic group A9 of positive results of 331, the average value of the index of virus concentration is 4.33±0.08 lg of HPV per 100 thousand cells, the minimum value in the analyses was 0.03 maximum 9.84 (p=0.008) (Fig. 2).

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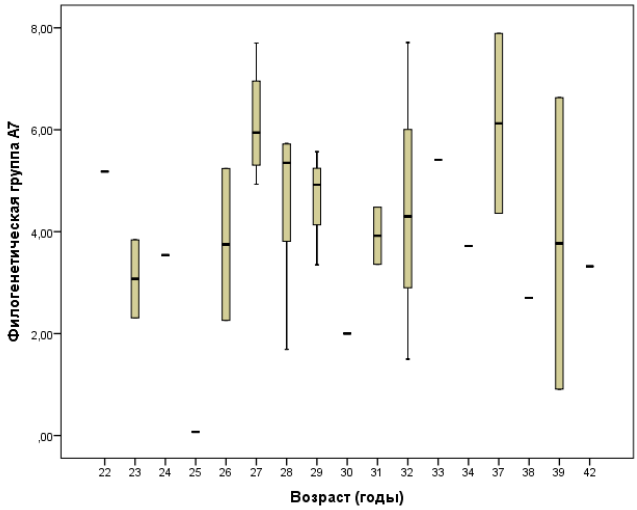

Fig.3. Distribution of HPV concentration of phylogenetic group A7 infection depending on age.

In the phylogenetic group A7 of positive results 508, the average value of the index of HPV concentration per 100 thousand cells is 3.39±0.09 lg, which is the minimum value in the analyses was 0.02, maximum 9.88 (p=0.008) (Fig.3).

In the phylogenetic group A5/A6 positive results of 631, the average value of the virus concentration index was 3.18±0.09 lg HPV per 100 thousand cells, the minimum value in the analyses was 0.01 maximum 11.45 (p=0.001) (Fig.4).

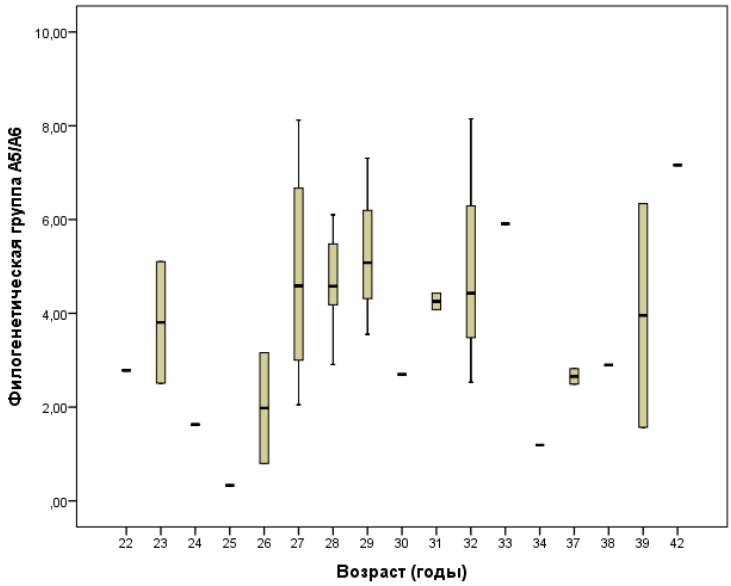

Fig.4. Distribution of HPV concentration index of phylogenetic group A5/A6 infection depending on age.

Despite the fact that the detection of HPV is different in all phylogenetic groups among age groups, the level of concentration fluctuations in each phylogenetic group was not statistically significant with age.

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It should be taken into account that infection of a person with a mono infection of one phylogenetic group is possible, but there are also co-infections by several phylogenetic groups. We analyzed the frequency of occurrence of different combinations of phylogenetic groups and the distribution of the index with the calculation of mean age.

According to the data obtained in our study, monoinfection of one phylogenetic group A9 was observed in 19.2%, group A7 in 23.3, and group A5/A6 in 33.8% of cases. There are combinations of phylogenetic groups: A9 and A7; A5/A6; A9 and A5/A6; A7 and A5/A6; A9, A7 and A5/A6. The most frequent is the combination of A5/A6, with 393 women accounting for 33.8% of the cases. The combination of A7 and A5/A6 was found in 167 women, accounting for 14.4 per cent of the cases. The combination of A9, A7 and A5/A6 was found in 167 women, representing 14.4 per cent of the cases. The combination of A9 and A7 was found in 37 women, accounting for 3.2% of the cases.

IV. DISCUSSION

The total number of analyses carried out was 6431, of which 1162 (18.1%) were positive. The dynamics of the absolute indicator of HPV infection detection by age of patients shows the highest level of HPV detection in different phylogenetic groups in the age groups: 18-24; 25-29; 30-34, with a gradual decrease in both the detection rate and the number of patients under investigation. This confirms the data obtained in Russia, where signs of HPV infection are detected in 15.0-34.4% of women over 19 years of age, and among patients who have applied for laboratory HPV diagnosis, the share of HPV infection reaches 44.9%, with suspected sexually transmitted diseases [1, 2]. The prevalence among age groups in Uzbekistan repeats HPV epidemiology on a global scale, when the risk of HPV infection increases from the age of sexual activity of women, the level of HPV detection increases, reaches its maximum at the age of 25-35 years, and then there is a decrease in the detectability of this indicator.

The age distribution of each phylogenetic group repeats the overall distribution of HPV detection, with an increase in detection rates under 20 years of age, a maximum of under 30 years of age, and a gradual decline thereafter. At the same time, there are no significant differences in the age distribution, apart from the general level, between the groups. The results obtained in our study confirm the data of Russian scientists, where 63.3% of the examined patients were found to be between 16 and 30 years of age and 25.6% -30 years of age and older [2]. It is known that HPV is one of the markers of women's sexual activity, so our data is a confirmation of this. The peak of HPV detection is under 18-35 years of age. After 35 years of age, viruses are less frequently diagnosed and there is a gradual decrease in detectability.

The results of the prevalence estimation of different phylogenetic groups are confirmed. The most common types of HPV with high oncogenic risk worldwide are types 16, 18, 31, 33 and 45 [6, 7], but the most common type in our study is A5/A6 (51 and 56 types). This determines the strategy for implementing preventive measures to prevent HPV by vaccinating girls aged 9-13 and introducing screening of women of fertile age to prevent cervical cancer [5, 11].

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V. CONCLUSIONS

HPV prevalence is similar to the global HPV epidemiology, with the risk of HPV infection increasing from the age of sexual activity for women, the level of HPV detection increasing, reaching a maximum between the ages of 25 and 35, and then decreasing.

Phylogenetic group frequency estimates have shown the following results: the most common types are A5/A6 (51 and 56 types) in 631 (54.2±1.4) cases, A7 in 508 (18, 39, 45, 59 types) (43.6±1.4) cases, A9 (16, 31, 33, 35, 52, 58) in 331 (28.4±1.3) cases, with statistically significant differences ($p<0.001$).

This distribution determines the strategy for the implementation of preventive measures aimed at preventing HPV prevalence by vaccinating girls aged 9-13 and introducing screening of women of fertile age to prevent the development of CC [5, 10, 11].

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