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PAPILLOMAVIRUS INFECTION AND CERVICAL CANCER INCIDENCE IN PRE-VACCINATION AND THE INITIAL VACCINATION PERIODS IN THE REPUBLIC OF SAKHA (YAKUTIA)

Summary

The research aims at studying patterns and regional characteristics of morbidity and incidence of various papillomavirus infection and cervical cancer forms in the Republic of Sakha (Yakutia) in the pre-vaccination period and the first years of vaccination against this pathology. It is established that the studied periods do not show any significant differences or decreasing trend in anogenital (venereal) warts morbidity. The study revealed higher (by 1/6-2 times) incidence of high-risk HPV of type 16 in women, compared with men. There was no decrease in type 16 and 18 HPV incidence in 2008-2011 (the period of introducing low vaccination coverage), compared with the year 2007. There is a trend for increased CC morbidity in women aged 30-44 years.

Key words: human papillomavirus infection, cervical cancer, morbidity, prevalence, vaccination

Introduction

In the early 1980s researchers managed to identify types of human papillomavirus (HPV) directly responsible for development of the oncologic process [1, 5, 6]. Harald zur Hausen was the first to suppose that HPV causes cervical cancer (CC) [10]. Nowadays, cancer-risk HPV types are recognized to provoke CC etiopathogenesis; moreover, they are responsible for development of vulvar cancer (20%), vaginal cancer (80%), penile cancer (40%), and anal cancer (90%); there is research being done to study the influence of cancer-risk HPV types on development of guttural and buccal cancers. Out of over 100 HPV types known today, 15 types have the oncogenic potential, and 8 (16, 18, 45, 31, 33, 52, 58, 35) are involved in 90% of CC cases, with types 16 and 18 HPV occurring in up to 70% of cases. Type 6 and 11 HPV are responsible for development of genital condylomas (anogenital (venereal) warts) in 90% of cases [1]. Our country's professionals in different fields have worked out principles of the laboratory diagnostics, epidemiological monitoring and prevention of papillomavirus infection and malignant growths related to this infection [2, 3, 4]. The study of mechanisms of carcinogenesis, induced by high-risk human papillomavirus infection (HR HPV), as well as the introduction of vaccines for preventing the

infection, caused by human papillomavirus of 6, 11, 16 and 18, has created conditions for decreased externalia condylomatosis morbidity and potential decrease in CC [7, 8, 9]. Papillomavirus infection has a number of peculiarities: variety of the virus genotypes and cancerogenic activity, polymorphism of clinical manifestations, chronic forms, dominance of symptom-free infections, primarily sexual transmission – they all call for a specific epidemiological monitoring system, which is to be developed under vaccination against the disease.

The aim of the research was to study patterns and regional characteristics of the morbidity and incidence of various papillomavirus infection and cervical cancer forms in the Republic of Sakha (Yakutia) in the pre-vaccination period and the initial years of vaccination against this infection.

Materials and Research Methods

We used methods of clinical, laboratory and epidemiological diagnostics. We analyzed the anogenital (venereal) warts morbidity in the years 1999-2011, the data being taken from forms of the state statistical observation that, in accordance with order of the Ministry of Health of the Russian Federation, are filled in by all derma-venereologic institutions. Also, we compared the prevalence of HPV of types 16 and 18 in 2007 (pre-vaccination period) and 2008-2011 (the period of the initial vaccination against HPV infection) in the Republic of Sakha (Yakutia). Using materials of the Republic's Oncology Center, we examined the morbidity trends, CC prevalence and mortality from the disease in the female population of the republic in 2000-2011. For laboratory diagnosis of human papillomavirus infection, caused by HPV of types 16 and 18, there was used the method of polymerase chain reaction (PCR) in the real time format and a number of locally-produced reagents: AmpliSens HPV 16/18-FL, AmpliSens HR HPV screen-FL, permitted for the use in the Russian Federation in the due order. There was a survey of patients having addressed the National Skin and Venereal Diseases Clinic and the Republic's Hospital of the Republic of Sakha (Yakutia). The material for the study was scraping of the mucous membrane epithelium from the cervical canal and urethra, taken by a universal urethral probe or a cytobrush. Among the patients examined, there were ones infected with sexually transmitted diseases (gonorrhea, anogenital warts), other sexually transmitted infections, inflammatory diseases of the urinary tract lower parts, as well as ones surveyed for preventive reasons, the patients with active sexual life. The total number of examinees in 2007-2011 amounted to 16,298 males and females.

Results and Discussion

The anogenital (venereal) warts morbidity in the Republic of Sakha (Yakutia) is distributed

unevenly over the years; thus, we made calculations and comparison of the average three-year data in the pre-vaccination period and the initial vaccination period (Fig. 1). The research showed that in 1999-2007 the morbidity varied from 21.7 to 34.0 per 100,000 of the population. In 2008-2010, the indicator remained at the 2005-2007 level (21.4 per 100,000 people). In 2011 there was an increase in morbidity (26.0 per 100,000 people). It should be noted that the republic used only the bivalent vaccine against HPV of types 16 and 18. In 2008, 2009, 2010 and 2011, the number of vaccinated women aged 10-30 years was 65, 70, 60 and 100 people, respectively. Therefore, there is no reason to expect a decrease in the incidence of this HPV infection form, which is caused predominantly by HPV of types 6 and 11.

The prevalence of HR HPV of type 16 and 18 in the Republic of Sakha (Yakutia) in 2007 and 2008-2011 is presented in Table 1. The results showed that, in general, type 16 HPV was found in 10.1% of the patients examined, type 18 HPV was found 2.6 times as less often - 3.9%. In 2011, there was an increase in type 16 HPV prevalence, compared with the year 2007, but the differences were not statistically significant ($p > 0.05$).

The frequency of HR HPV detection in female patients was 1.6-2 times higher than in males (Fig. 2). These data should be considered when analyzing the cancer morbidity associated with HR HPV in men and women.

Important results were obtained in the study of the prevalence of types 16 and 18 HPV in different age groups of the female population. Even children, who become sexually active early, were infected with HR HPV (Fig. 3). The highest prevalence of type 16 HPV were found in women aged 15-19 and 20-29 years, which corresponds to the age structure of the CC patients in the recent years.

The problem with cervical cancer in the Republic of Sakha (Yakutia) is one of the most serious health problems. In 2010 – 2011, this pathology ranked third in the female cancer structure, having ranked fourth in the year 2000. Annually, the republic registers from 67 to 106 new cases of the disease. The morbidity tends to increase: the 2011 indicator was significantly higher compared with the year 2000 (20.4 and 13.9 per 100,000 of the female population, respectively). The CC prevalence and mortality of this disease are relatively high. Fig. 4 shows the results of the studying the cervical cancer morbidity in different age groups of the female population of the Republic of Sakha (Yakutia) in 2000 and 2011. There is a shift of the morbidity towards younger age groups, with the increased incidence rate in reproductive-age women aged 30-34 (by 1.3 times), 35-39 (by 2.7 times) and 40-44 years (by 3.2 times); and it is traditionally high in persons over 60 years.

Conclusion



The results showed a high relevance of human papillomavirus infection and cervical cancer in the Republic of Sakha (Yakutia). For the first time, the study established patterns of the epidemic processes caused by high and low cancer risk HPV, and regional characteristics of the infection in the pre-vaccination period and the initial stage of vaccination against this disease. We determined age and sex characteristics in the prevalence of HR HPV of type 16 and 18. There was established a relation between the high prevalence of HR HPV in women aged 15-29 years and the changed age structure of cervical cancer patients, in particular, the increase in morbidity in the age group 34-44 years, which corresponds to the published data, indicating the range of about 10 years between the moment of being infected with HR HPV and development of cervical cancer. In general, the results of the study show that the republic needs to establish the epidemiological monitoring system over human papillomavirus infection, and the present study outlines main principle thereof. The results of the study can contribute into development of the Regional Vaccination Calendar and Vaccination Financing Plan, with HPV vaccination being included therein.

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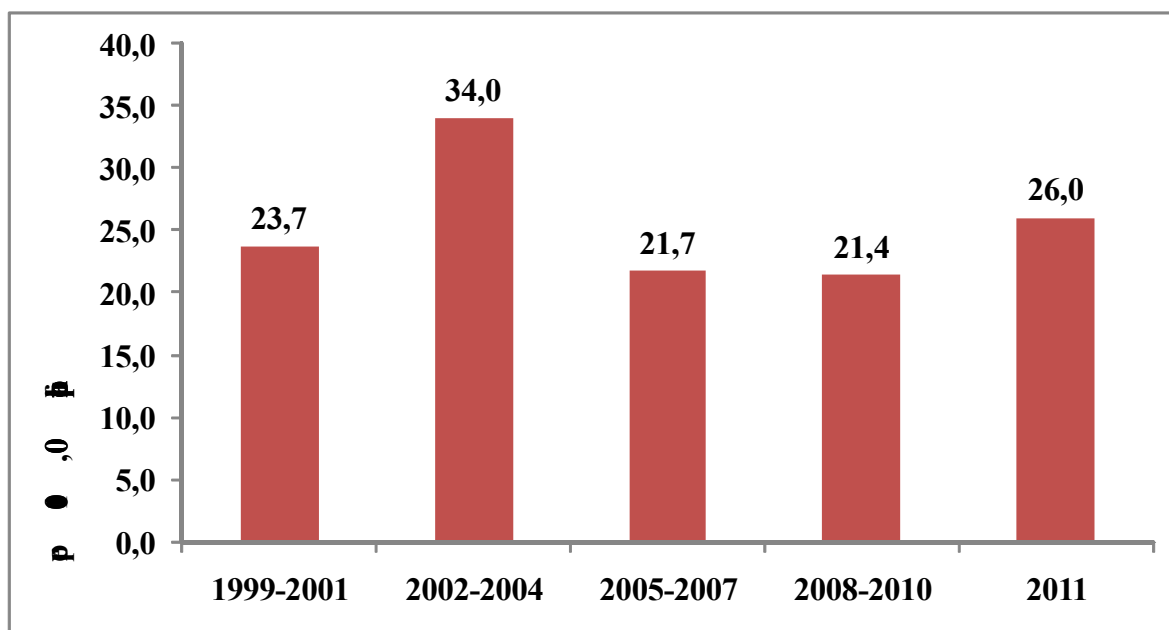


Fig. 1. Anogenital (venereal) warts morbidity (ICD-10 - A63.0) in the Republic of Sakha (Yakutia), 1999-2011.

Table 1.

Type 16 and 18 HPV detection rate in the Republic of Sakha (Yakutia) in 2007-2011.

Year	Number of the examined	HPV 16		HPV 18	
		Abs. number	% $\pm$ m	Abs. number	% $\pm$ m
2007	710	69	9.7 $\pm$ 1.1	35	4,9 $\pm$ 0,8
2008	2,234	182	8.2 $\pm$ 0.6	80	3,6 $\pm$ 0,4
2009	4,140	434	10.5 $\pm$ 0.5	149	3,6 $\pm$ 0,3
2010	3,376	322	9.5 $\pm$ 0.5	113	3,4 $\pm$ 0,3
2011	5,838	644	11.03 $\pm$ 0.4	256	4,4 $\pm$ 0,3
Total for 5 years	16,298	1,651	10.1 $\pm$ 0.2	633	3,9 $\pm$ 0,2

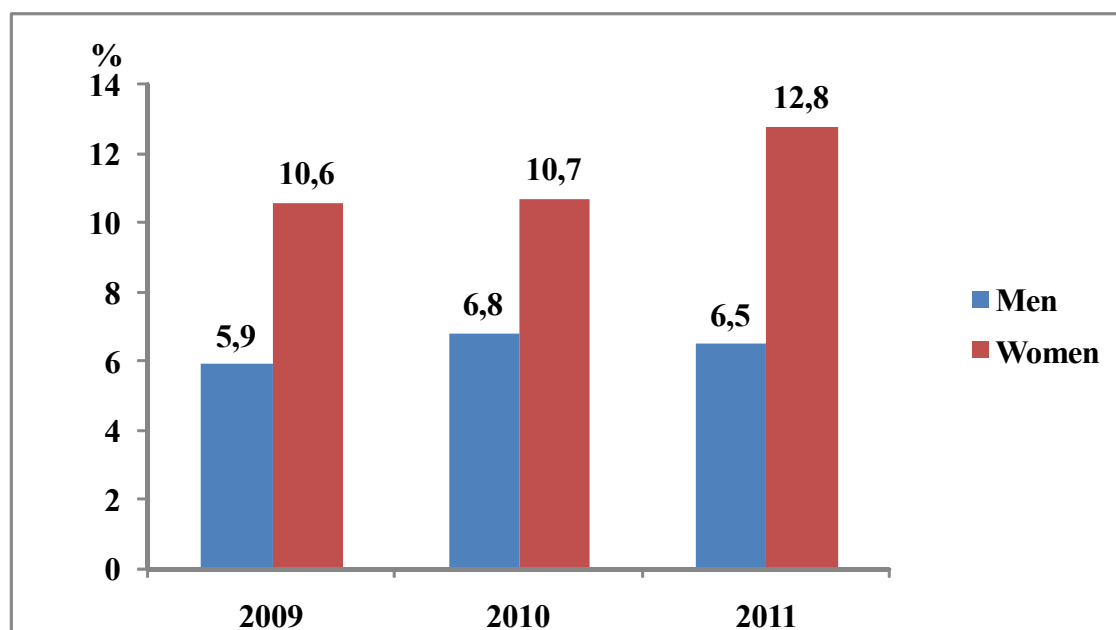


Fig. 2. Detection rate for high-risk HPV of type 16 in men and women in the Republic of Sakha (Yakutia) in 2009-2011 (per 100 examined people)

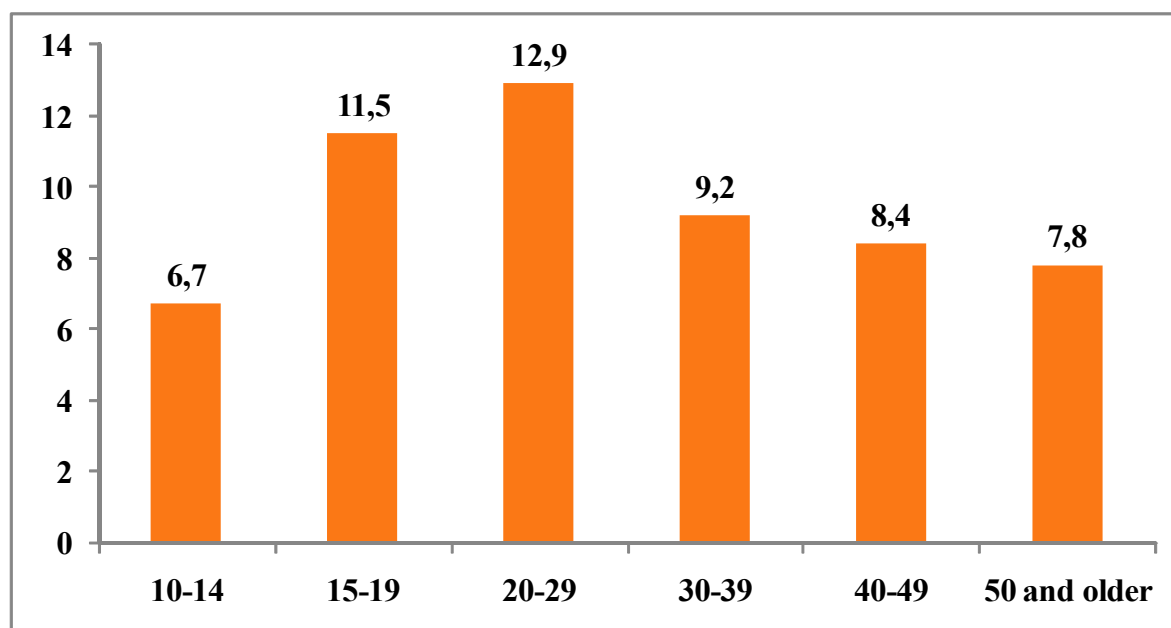


Fig. 3. Type 16 HPV incidence for various age groups of women in the Republic of Sakha (Yakutia) in 2007-2011 (per 100 examined people)

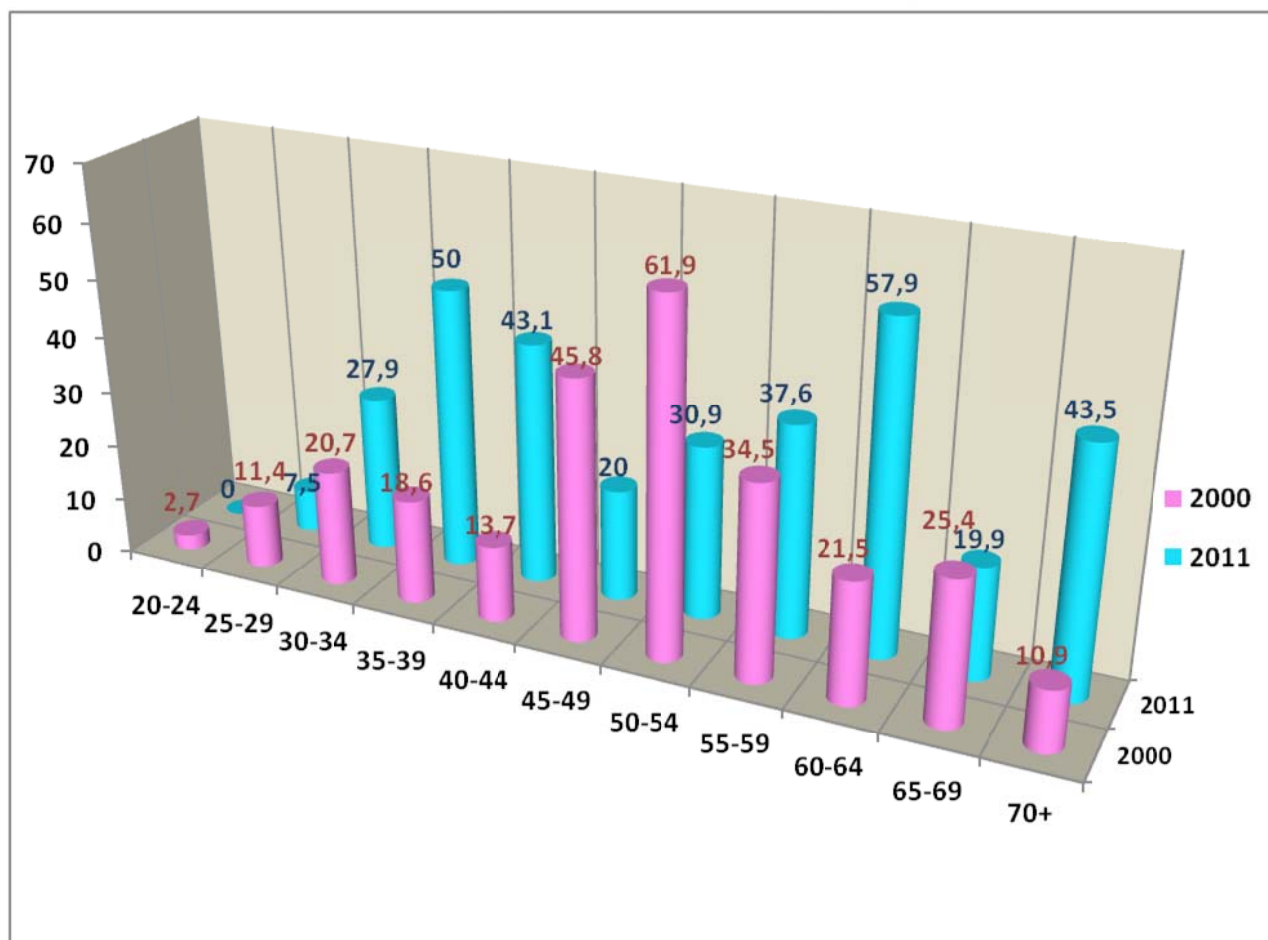


Fig. 4. CC morbidity in various age groups of the female population in the Republic of Sakha (Yakutia) in 2000 and 2011 (per 100,000)