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# Early Diagnostics and Treatment of HPV-Associated Precancer Diseases of the Cervic

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**Abstract** Cervical cancer is one of the few cancers that can be prevented. When it is diagnosed at an early stage, the disease is more amenable to effective treatment, which increases overall and relapse-free survival, improves the quality of life of patients, and reduces the cost of treatment. According to international guidelines, Human Papillomavirus (HPV) DNA tests represent a valid alternative to Pap Test for primary cervical cancer screening, provided that they guarantee balanced clinical sensitivity and specifcity for cervical intraepithelial neoplasia grade 2 or more (CIN2+) lesions. The study aimed to assess whether HPV Selfy (Ulisse BioMed – Trieste, Italy), a full-genotyping HPV DNA test that detects and diferentiates 14 high-risk HPV (HR-HPV) types, meets the criteria for primary cervical cancer screening described in the international guidelines, on clinician-collected as well as on self-collected samples.

**Keywords** Diseases of the cervix, Oncogenic types of HPV, Early diagnosis

## 1. Introduction

Pathology of the cervix (CC) is one of the most common gynecological diseases, especially in antenatal clinics - 25-45%. In gynecology and obstetrics, early diagnosis and adequate treatment of background and precancerous diseases, as well as initial forms of cervical cancer, remain one of the most important problems [1]. Cervical cancer (CC) is a major public health problem in Uzbekistan. According to the International Agency for Research on Cancer IARC (IARC) estimates for 2018, cervical cancer is the second most common type of cancer among women in Uzbekistan after breast cancer and the third most common cause of death of women from cancer in Uzbekistan. According to estimates for 2021, the age-standardized incidence and mortality rates are 5.3 and 2.9 per 100,000 women per year, respectively. According to the national cancer registry, in 2021 in Uzbekistan, the number of initially diagnosed cases of cervical cancer in the republic was 1827, 997 cases of death from cervical cancer were registered with the following distribution of cases by stages: stage-I: 12%, stage-II: 54, 1%, stage-III: 23.6%, stage-IV: 5.3%. Every year in Europe, more than 25,000 cases of cervical cancer are diagnosed and about 12,000 deaths from this disease, which exceeds the number of deaths from AIDS and hepatitis combined [2,3]. The etiological link between persistent HR-HPV infection and the development of high-grade cervical dysplasia and cervical cancer is well established. The two oncogenic HPV types that most commonly cause cervical cancer are types 16 and 18. Together they cause approximately 70% of cervical cancers. of the uterus in all countries of the world, unfortunately, the incidence of cervical cancer prevails in developing countries. CC is one of the few cancers that can be prevented [2,4]. Early diagnosis of precancer provides for the possibility of primary and secondary prevention. Primary prevention is a system of measures to identify risk factors for the development of cervical cancer and eliminate them. This is primarily the promotion of a healthy lifestyle, increasing the education of the population, the fight against smoking, the use of barrier methods of contraception, the prevention and identification of risk factors for the spread of human papillomavirus infection (PVI) and other sexually transmitted infections (STIs), the development and implementation of preventive vaccines. Secondary prevention is cervical screening, that is, examination of all women in order to detect changes in the cervical epithelium and timely treatment of precancer and cervical cancer [5].

Cervical cancer of the brand is one of the few forms of malignant neoplasms that satisfy all the requirements of population screening, i.e. is an almost completely preventable disease [4,5]. The Regional Consultative and Diagnostic Center has accumulated 10 years of successfull experience in identifying, treating and monitoring patients with cervical pathology, i.e. with background and precancerous processes (Anisimova, N.S., 2014., Zaletaev / (.V., Nemtsova M.V., Bochkov T.P. 2012). Algorithms for diagnosing monitoring of patients have been developed. Improvement of screening programs and methods of early diagnosis of precancerous diseases of the cervix contributes

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to the prevention of invasive cervical cancer.

According to WHO, about 450 thousand new cases of cervical cancer (CC) are registered annually in the world. Annually in the countries of the European Community there are more than 25 thousand new cases of diseases and about 12 thousand deaths. deaths associated with them (Klipyshkova, T.V., 2013, Mindlina, A.Ya., 2013). In recent years, in economically developed countries, there has been an increase in the incidence of cervical cancer among women under 40 years old [6]. second place after breast cancer. CC was one of the leading causes of death several decades ago in many countries. The introduction of the cytological screening method in the USA, Europe, Australia over the past 40-50 years has reduced the incidence of cancer by 80-90%. It is believed that if all preventive and treatment measures are taken in a timely manner, then 90% survival can be achieved with cervical cancer (Belokrinitskaya, T.E. 2007, Kiselev V.I., Ashrafyan L.A., Budarina S.O., Kiselev O.I., Paltsev M.A., Kulakov V.I., Prilepskaya V.II. 2014). In our country, there is cytological screening, which is available to women free of charge at the place of residence. Most often, women turn to take a cervical smear of their own free will or accidentally when contacting a gynecologist for another issue. Various methods are used in the diagnosis of precancerous diseases and cervical cancer, but the most accessible for practice are the clinical-visual method, the use of colposcopy, molecular biological research methods (PCR or DIGENE test.) and morphological studies. The combined use of these methods and new laboratory technologies with the determination of E7 and pl6ink4a biomarkers for the early diagnosis of cervical diseases will make it possible to detect oncopathology at the initial stages of development. Pathology of the cervix is one of the most common gynecological diseases, especially in antenatal clinics 25-45%. Papillomavirus infection (PVI) is one of the most common sexually transmitted infections that occurs in most of the world's sexually active population. According to modern concepts, the human papillomavirus (15114) is considered as an etiological factor in the development of cervical dysplasia, and long-term persistence of HPV contributes to the occurrence of relapses or malignant transformation of lesions.

Cervical cancer occupies the 2nd place in the structure of oncological morbidity in women and today is considered as a pathology of the cervix associated with the human papillomavirus [6,7]. In general, in most countries the incidence of cervical cancer does not tend to decrease, in Russia it remains higher than in developed countries, and the maximum number of cases in Siberia and the Far East Poletaev D.V., Nemtsova M.V., Bochkov II. 11.2012, Arbyn M, Raifu AO, Weiderpass K, Bray l\ Anttila A. 200), The development of cervical cancer is not a lightning-fast process: according to WHO, the transition from dysplasia to cancer in situ lasts an average of 3-8 years, another 10-15 years pass before the development of microinvasive cancer and the same amount before the transition to a common form. Thus, the doctor has enough time to identify the initial forms of the disease (Gretsova, O.P., 2009, Kogan E.A., Faizullipa N.M. Li Ts. et al. 2014, Dalerba R., Cho R. W. Clarke M.F., 2017). The maximum HPV infection occurs at the age of 18–25 years and decreases after 30 years, when the incidence of dysplasia and cervical cancer increases significantly, the peak of which occurs at 45 years [7]. Despite the fact that among all malignant neoplasms, cervical cancer is a disease in relation to which preventive measures have been the most successful, it is still an important medical and social problem (Gretsova, O.P. 2009, Kogan E.A., Fayzullina N.M., Li 1 (et al. 2014). Debatable remains the informativeness of screening methods for diagnosing dysplasia and cervical cancer [9], among which the cytological method is considered the leading one, which, with the correct sampling of material, can detect tumor changes in 94.5% of cases (Kuznetsov S.L. Muptkambarov II.II. 2015. The need to introduce methods for determining HPV DNA is under active discussion. In gynecology and obstetrics, early diagnosis and adequate treatment of background and precancers diseases, as well as the initial forms of cervical cancer, remain one of the most important problems (Aksenova, S. 11. 2017).

Various methods are used in the diagnosis of precancerous diseases and cervical cancer (CC), but the most accessible for practice are the clinical-visual method, the use of colposcopy, molecular biological methods for detecting NVI (polymerase chain reaction - PCR), cytological examination of smears and histological examination targeted biopsy of the cervix.

Summarizing the information presented, it should be noted that diagnostics aimed at predicting the pathology of the cervix should be based on the cytological method, supported by PCR diagnostics of the human papillomavirus and the introduction of molecular biomarkers [10]. Methods for early diagnosis and the introduction of new screening technologies for diseases of the cervix open up additional opportunities for the prevention of cervical cancer, which is the basis for reducing diseases in general and opens up prospects for maintaining women's health.

**Target.** Improving the early diagnosis and treatment of precancerous HPV-associated cervical intraepithelial neoplasias using a modified screen tester and radiosurgical destruction.

## 2. Material and Research Methods

Total number of patients within 240: Age category 30-55 years, divided into 2 groups: Group 1 (main) is also divided into 3 subgroups:

A) Patients with pathologically unchanged cervical mucosa;
B) Patients with background and inflammatory diseases of the cervix;
C) Patients, with CIN1, CIN2, CIN3 Results. All the studied patients underwent screen tests using the self-collection method (Quintip), the results of which

were evaluated according to the criteria. Analysis of test results showed the following results: CIN1 - 50 (33.3%), CIN 2-15 (12.5%), CIN 3-10 (8.3%), cervical cancer - 5 (4.1%), underlying diseases of the cervix 35 (29.1%) and 15 (12.5%) women without pathological changes, i.e. negative result.

## 3. Conclusions

Background and precancerous diseases of the cervix associated with papillomavirus infection occur mainly in the age group of women aged 15-25 years, sexually active, having several sexual partners. Quintip Modified Staining Solution has the advantages of availability, cost-effectiveness, low technical requirements, safety and non-invasiveness, as a result, it can be successfully applied in the practice of primary care and in remote regions of the country. HPV Selfy fulflls all the requirements of the international Meijer's guidelines and has been clinically validated for primary cervical cancer screening purposes. Moreover, HPV Selfy has also been validated for self-sampling according to VALHUDES guidelines. Therefore, at date, HPV Selfy is the only full-genotyping test validated both for screening purposes and for self-sampling.

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