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Introduction into Practice Methods of Early Diagnostics in Diseases of the Cervic

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Abstract: Cervical cancer (CC) is considered to be one of some oncological diseases, which, when diagnosed at an early stage, can be effectively treated, which increases overall and recurrence-free survival, improves the quality of life of patients, and reduces the cost of treatment. The cause of cervical cancer is the human papillomavirus (HPV) of oncogenicgenotypes, which can be prevented by screening tests.

Keywords: diseases of the cervix, oncogenic types of HPV, minimally invasive methods, early diagnosis.

Introduction. 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, age-standardized incidence and mortality rates are 5.3 and 2.9 per 100,000 women per year, respectively.[1, 2] Cervical cancer is the fourth most common tumor in women worldwide, with estimated 569.847 new cases and 311.365 related deaths per year [1]. In the last decades, cervical cancer-related mortality dramatically decreased, thanks to the widespread use of screening programs [2]. Cervical cytology has been used for years as standard test for cervical cancer screening [3]. However, it has some potential limitations: conventional staining procedure requires a considerable amount of time and consumables; smearing process of the Pap test is characterized by poor reproducibility [4]; errors in the interpretation of the results can be caused by blood and mucus, imperfection in the fixation or by a non-uniform distribution of cells on the slide [5]. Moreover, it requires a gynecologist (or midwife) to be performed and a cytologist to be analyzed, with an increase in costs and the necessity of a proper setting. The development of this disease is not associated with the presence of known hereditary syndromes. The cause of cervical cancer is the human papillomavirus (HPV) of oncogenic genotypes [1, 2]. Most patients with cervical cancer have HPV 16 and/or 18 of the oncogenic genotype [3]. As risk factors for the development of this pathology, the following are considered: early onset of sexual activity, frequent change of sexual partners, refusal of contraceptives of the "barrier" type, smoking, immunosuppression, the issue of the influence of various sexually transmitted infections is discussed [4, 5]. -registry, in 2021 in Uzbekistan, the number of initially detected 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, more than 25,000 cases of cervical cancer are diagnosed in Europe and about 12,000 deaths from this disease are diagnosed, which exceeds the number of deaths from AIDS and hepatitis combined. The etiological relationship between persistent HR-HPV infection and the development of high-grade cervical dysplasia and cervical cancer is well known. The two oncogenic HPV types that

most commonly cause cervical cancer are types 16 and 18 [7]. Together they cause approximately 70% of cervical cancer cases in all countries of the world, unfortunately, the proportion of cervical cancer incidence prevails in developing countries. CC is one of the few cancers that can be prevented [9] . 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 epithelium of the cervix and timely treatment of precancer and cervical cancer.[13] Clinical manifestations of CC are abundant watery leucorrhoea and "contact" bloody discharge from the genital tract. In women of the reproductive period of life, acyclic and contact bleeding from the genital tract may appear, in the postmenopausal period - periodic or permanent. With a significant local-regional spread of the tumor, pain, dysuria and difficulty in defecation appear.[12]

Material and research methods. Various methods are used in the diagnosis of precancerous diseases and cervical cancer: clinical-visual; extended vulvovaginal and colposcopy; cytological; liquid cytology; molecular genetic (viral genotyping, expression of viral oncoproteins E6, E7); determination of viral load Hybride Capture (Digene-test); morphological study; immunocytochemical and immunohistochemical study of markers p16, Ki67; optical-electronic scanning of cervical tissue (TruScreen); anoscopy (using a colposcope). Our study included 130 patients with pathological changes in the cervix of varying degrees associated with HPV, such as cervical intraepithelial neoplasia (CIN) and underlying cervical disease. We used a minimally invasive method in the form of a CIN-DIAG solution, which has a sensitivity of 98% and a specificity of - 95% to determine pathological changes in the early stages of development. It is a sterile test tube, inside of which there is a tupfer (a long spatula with a cotton / viscose swab at the end). The clinical sensitivity and specificity of the CIN-DIAG solution proved to be no worse than other methods. In an analysis of a total of 130 cervical cytological specimens from the screening population, of which 58 were from women with CIN2+, the test showed a relative sensitivity and specificity for CIN2+ of 0.98 and 1.00, respectively. HPV-based screening can detect persistent high-grade cervical lesions prior to conventional cytology, providing 60–70% greater protection against invasive cervical carcinomas compared to Pap smear [11]. In addition, we have demonstrated that the performance of the CIN-DIAG test on self-collected vaginal specimens is as good as that obtained on clinician-collected cervical specimens (relative sensitivity 0.92 and relative specificity 0.97). Finally, with this method we will be able to describe the prevalence of HPV types in the study population.

Results. The solution enters the cell with the help of folic acid through a specific effect on cell surface receptors. As a result of a specific reaction of the dye solution with the chemical substance of the histiocyte, the tampon is stained. In normal cells, there is a low content of active oxygen, so there is little expression of folic acid receptors on the cell surface and there is no staining of the tampon after the reaction. Analysis of the test results showed the following results: CIN1 - 32 (33.3%), CIN 2 - 58 (12.5%), CIN 3 - 12 (8.3%), cervical cancer - 8 (4.1%) , background diseases of the cervix 70 (29.1%) and 30 (12.5%) women without pathological changes, i.e. negative result.

Discussions. Cervical cytology has been used for many years as the standard screening test for cervical cancer. However, it has some potential limitations: the conventional staining procedure requires a significant amount of time and consumables, and the Pap smear smear process is characterized by poor reproducibility and errors in interpretation due to blood and slime[6,14]. Moreover, it requires a cytologist for analysis, with increased costs and the need for a proper parameter. HPV-based screening helps detect persistent high-grade cervical lesions prior to

conventional cytology, providing 60% to 70% greater protection against invasive cervical carcinomas than a Pap smear. CIN-DIAG solution may be an attractive solution to increase participation in screening for opportunistic cervical cancer regardless of age, educational level, and other possible social parameters. To the question "Was the procedure easy?" 98.26% of women answered in the affirmative.

Conclusion: This minimally invasive method for early detection of cervical cancer complies with all international guidelines and has been clinically tested for primary screening of cervical cancer and has been approved for self-sampling.

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