

## DIAGNOSTICS AND TREATMENT OF CERVICAL INTRAEPITHELIAL NEOPLASIA IN PREGNANT WOMEN

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**Abstract.** The article describes the methods of diagnosis and treatment of pregnant women with intraepithelial neoplasia of the cervix.

**Keywords:** neoplasia, cervical cancer, pregnancy, biopsy, extragenital diseases, CIN, HPV, ectopia, endocervix, exocervix.

## ДИАГНОСТИКА И ЛЕЧЕНИЕ ИНТРАЭПИТЕЛИАЛЬНОЙ НЕОПЛАЗИИ ШЕЙКИ МАТКИ У БЕРЕМЕННЫХ

**Аннотация.** В статье описаны методы диагностики и лечения беременных с интраэпителиальной неоплазией шейки матки.

**Ключевые слова:** неоплазия, рак шейки матки, беременность, биопсия, экстрагенитальные заболевания, CIN, ВПЧ, эктопия, эндоцервикс, экзоцервикс.

**Relevance:** Invasive cervical cancer ranks first among gynecological tumors associated with pregnancy and is detected, according to various authors, in an average of 0.8-1.2 per 10,000 pregnancies. Cervical cancer detected within 6 months after termination of pregnancy and 12 months after childbirth refers to tumors associated with pregnancy, since clinical and morphological manifestations of the tumor process are already present during pregnancy. Among patients with cervical cancer, the frequency of combination with pregnancy is 1-3%.

**Purpose of the study:** to identify clinical and morphological features of cervical intraepithelial neoplasia associated with pregnancy in order to optimize the diagnosis and treatment of the disease.

**Materials and methods of research:** The material for the study was the clinical and morphological data of 110 patients observed in the Bukhara branch of the Republican Specialized Oncology Scientific and Practical Center with a diagnosis of intraepithelial neoplasia of the cervix. with pregnancy. Examination and treatment were carried out from 2010 to 2023.

The study analyzed anamnestic, clinical, morphological, including immunocytochemical, immunohistochemical, and molecular data. In order to obtain the necessary information, outpatient cards of patients were studied, cytological samples and histological sections of biopsy tissue were reviewed using the pathomorphological classifications of CIN and Bethesda system. In clinical groups, information was recorded on the average age of menarche, sexual debut,

contraceptive behavior, reproductive history, past gynecological and extragenital diseases. Verification of the diagnosis and cytological monitoring were performed using traditional and liquid cytological examination of the exocervix and endocervix epithelium. Using immunohistochemical and immunocytochemical methods, qualitative features of markers of proliferative and antiproliferative activity Ki-67 and p16 in CIN in pregnant women were studied. For this purpose, histological examination with immunohistochemical analysis was performed on cervical biopsies during pregnancy (n=23), postoperative material (n=57), namely, scrapings from the cervical canal and cones of the resected cervix after childbirth or termination of pregnancy. Immunocytochemical analysis of CINtec PLUS on a VENTANA stainer was performed on samples with BD SurePath liquid medium (n=10). Using the polymerase chain reaction method, the frequency of HPV infection among women with CIN in combination with pregnancy was revealed. The risk of oropharyngeal colonization with HPV in children of HPV-infected mothers was determined. For this purpose, a group of children born to HPV-infected women suffering from cervical intraepithelial dysplasia during pregnancy was identified, which was represented by 10 newborns up to 2 days from birth and 20 children aged 1.1 to 3.4 years. As a result of the study, the course and outcome of the disease during pregnancy, after delivery or termination of pregnancy were analyzed.

### CONCLUSIONS:

The average age of pregnant women with CIN was  $29.3 \pm 4.3$  years: CIN1/LSIL -  $27.4 \pm 3.8$  years, CIN 2-3/HSIL -  $30.0 \pm 3.6$  years, including: primiparous - 64.3%, with aggravated gynecological history - 44%, with cervical ectopy - 67%, infected with human papillomavirus - 79.6%. Cytological examination is an effective method for diagnosing and monitoring pregnancy-associated CIN. The sensitivity of the method was 97.9%. Immunocytochemical study (ICC) "double staining" is an additional method in the diagnosis and prognosis of CIN (in all cases of a negative result of ICC "double staining" regression of the disease was observed after childbirth). Predictive factors for an unfavorable prognosis of CIN were: age over 27 years (persistence rate - 66% versus 38% in pregnant women under 27 years,  $p_{TCF} < 0.05$ ); severity of dysplasia: (with CIN3, the persistence rate is 78% versus 16% with CIN2,  $p < 0.001$ ); HPV-positive status (persistence rate is 70% versus 35% with HPV-negative status,  $p < 0.001$ ); the presence of cervical ectopy (persistence rate is 70.7% versus 29% in the absence of cervical ectopy,  $p < 0.001$ ); a positive result of immunocytochemical "double staining" (persistence rate of 100%). The type of delivery did not affect the "biological behavior" of CIN (the frequency of CIN3 persistence after delivery was 74% versus 85% after cesarean section,  $p = 0.072$ ). The peculiarity of the treatment tactics for women with CIN detected during pregnancy, if they want to continue the pregnancy, is cytological monitoring, per vias naturales delivery, repeated

itological examination 8 weeks after delivery (the frequency of progression to invasive cancer is 0.9%); if they do not want to continue the pregnancy - conization of the cervix 2 months after medical abortion. There is no risk of transmission of papillomavirus infection from mother to child. HPV DNA was not detected in any case among children born to HPV-infected mothers with CIN.

### **PRACTICAL RECOMMENDATIONS:**

If CIN is detected during pregnancy and there is a desire to continue the pregnancy, prolongation of pregnancy with regular cytological monitoring under the supervision of an obstetrician-gynecologist and oncologist is indicated. Immunocytochemical study of "double staining" is an additional method in the diagnosis and prognosis of the course of CIN, especially in controversial cases. Only in cases of suspected invasive process histological examination of tumor biopsy is indicated. The presence of CIN is not an indication for cesarean section.

All women who continue the pregnancy are recommended to have a repeat examination with cytological examination 2 months after delivery and subsequent electroconization of the cervix. In case of regression of CIN after delivery, conization of the cervix is indicated due to the risk of recurrence of CIN (up to 12.0%), however, it is possible to postpone conization for several subsequent months to minimize the risk of bleeding.

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