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ТИББИЁТДА ЯНГИ КУН НОВЫЙ ДЕНЬ В МЕДИЦИНЕ NEW DAY IN MEDICINE

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ANALYSIS OF THE RELATIONSHIPS BETWEEN THE RESULTS OF DIAGNOSTIC METHODS OF RESEARCHING THE PATHOLOGY OF DEVELOPMENT OF CERVICAL INTRAEPITHELIAL NEOPLASIA

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✓ Resume

The analysis of social-anamnestic risk factors and sexual behavior characteristics revealed highly reliable risk factors for the development of HSIL: smoking (4.375 times higher in the HSIL group than in the NILM group, $p<0.007$); body mass index (25.40 in the HSIL group, 23.95 in the NILM group, $p<0.027$); a large number of sexual partners (in the HSIL group there were on average 4 partners during their lifetime, in the NILM group 2 partners, $p<0.001$); early sexual debut (at the age of 16 in the HSIL group, 18 in the NILM group, $p<0.004$); the practice of unprotected sexual intercourse (6.769 times more frequent in the HSIL group than in the NILM group, $p<0.001$).

Keywords: cervix, human papillomavirus, intraepithelial neoplasia.

АНАЛИЗ ВЗАИМОСВЯЗЕЙ РЕЗУЛЬТАТОВ ДИАГНОСТИЧЕСКИХ МЕТОДОВ ИССЛЕДОВАНИЯ ПАТОЛОГИИ РАЗВИТИЯ ЦЕРВИКАЛЬНЫХ ИНТРАЭПИТЕЛИАЛЬНЫХ НЕОПЛАЗИЙ

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✓ Резюме

При анализе социально-анамнестических факторов риска и особенностей полового поведения выявлены высоко достоверные факторы риска развития HSIL: табакокурение (в группе HSIL выше в 4,375 раза по сравнению с NILM, $p<0,007$); индекс массы тела (в группе HSIL - 25,40, в группе NILM - 23,95, $p<0,027$); большое количество половых партнеров (в группе HSIL в среднем в течение жизни было 4 партнера, в группе NILM 2 партнера, $p<0,001$); ранний половой дебют (в группе HSIL в 16 лет, в группе NILM 18 лет, $p<0,004$); практика незащищенных половых контактов (в группе HSIL чаще в 6,769 раз по сравнению с NILM, $p<0,001$).

Ключевые слова: шейка матки, вирус папилломы человека, внутри эпителиальная неоплазия.

BACHADON BO'YNI INTREPITHELIAL NEOPLAZIYASI RIVOJLANISH PATOLOGIASINI TADQIQLASH USULLARI NATIJALARI O'RTASIDAGI BOG'LIKLIKNI TAHLIL QILISH

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✓ **Rezyume**

Ijtimoiy-anamnestic xavf omillari va jinsiy xulq-atvor xususiyatlarini tahlil qilish HSIL rivojlanishi uchun juda ishonchli xavf omillarini aniqlandi: chekish (HSIL guruhida NILM guruhiga qaraganda 4,375 baravar yuqori, $p<0,007$); tana massasi indeksi (HSIL guruhida 25,40, NILM guruhida 23,95, $p<0,027$); ko'p sonli jinsiy sheriklar (HSIL guruhida umr bo'yi o'rtacha 4 ta sherik bo'lgan, NILM guruhida 2 ta sherik, $p<0,001$); erta jinsiy debyut (HSIL guruhida 16 yoshda, NILM guruhida 18 yoshda, $p<0,004$); himoyalalmagan jinsiy aloqa (HSIL guruhida NILM guruhiga qaraganda 6,769 baravar ko'proq, $p<0,001$).

Kalit so'zlar: bachadon bo'yni, inson papillomavirusi, intraepitelial neoplaziya.

Relevance

The problem of cervical intraepithelial neoplasia (CIN) and cervical cancer (CC) has not lost its relevance for many years [1,3,5,7]. The incidence of cervical cancer remains stably high for a long time [2,4,6,8]. The incidence of cervical intraepithelial neoplasia is several times higher than the prevalence of cervical cancer and annually reaches 30 million new cases of low-grade squamous intraepithelial lesions (LSIL) and 10 million high-grade squamous intraepithelial lesions (HSIL) [2,9,10]. In 2023, the incidence of cervical cancer per 100 thousand population was 128.7, 15,303 new cases were identified [1,11,13,15]. In 2021, cervical cancer was the leading cause of cancer mortality among women aged 25-29 [1,12,14]. This fact ultimately negatively affects the birth rate, the increase of which is a priority in Uzbekistan. Recurrence of precancerous cervical lesions after surgical treatment varies from 5 to 23%, this high rate also confirms the need to adjust the tactics of managing women with this pathology [1,2]. It is known that cervical cancer results from the effect of high-risk human papillomavirus (HPV-HCR) on epithelial cells [1,16,17]. HPV types 16 and 18, according to various authors, cause up to 82.5% of cervical cancer cases [18]. Among the sexually active population, HPV is the most common sexually transmitted infection [1,3,5,7]. Vaccination against HPV has been used since the beginning of the 21st century for the purpose of primary prevention. In countries with high vaccination coverage, there is already data on a long-lasting immune response after 10 years and a decrease in the incidence of cervical cancer [1]. However, despite infection with HPV, the oncological process does not occur in all women, but only under certain conditions [18]. Risk factors that contribute to the occurrence and progression of precancerous lesions of the cervix are identified. Among the triggers are age, smoking, infection with the human immunodeficiency virus, early onset of sexual activity, frequent change of sexual partners, autoimmune diseases, excess body weight, long-term use of hormonal contraceptives, and disruption of the cervicovaginal microflora. Data on the presence of influence and its degree vary [1,7]. In many studies, the role of age as a risk factor has not been confirmed [1,7]. However, in some, the risk of cervical dysplasia increased with age [18]. In the study by Bowden, S. J. et al. which included 273,377 women, the role of smoking and frequent change of sexual partners in the progression of CIN and the occurrence of cervical cancer is confirmed [1,21]. A meta-analysis of 45 studies conducted by Nagelhout G. et al. also confirms the role of smoking in carcinogenesis [1,3]. According to Korolenkova L.I., if a woman has had 5 or more sexual partners during her life, the risk of HPV infection is almost 100% [18]. In a study conducted in Japan involving 3968 women, the number of partners was not statistically significant in relation to the occurrence of severe cervical lesions [1,22]. Collins S. et al. It was found that in HPV-negative women with no intraepithelial lesions based on cytological examination, smoking and the number of sexual partners were not associated with the risk of HPV infection [1]. With the advent of new methods for diagnosing the microbiome and, as a result, the identification of new microorganisms, special attention is paid to the role of the microbiota of the reproductive system in the development of high-grade cervical intraepithelial lesions [18,19,20]. Imbalance of the local microbiota is the cause of HPV persistence and, as a consequence, accelerated oncotransformation of the epithelium [2]. Studies of the biological diversity of microorganisms and an assessment of symbiotic microbial communities are required to better understand the role of the microbiota in the development of cervical intraepithelial lesions. Correction of vaginal dysbiosis and identification of key bacteria may become a target for therapeutic interventions to prevent the occurrence and progression of cervical intraepithelial neoplasia. Eliminating the above-mentioned risk factors is secondary prevention and will help reduce the prevalence of precancerous cervical lesions. Despite numerous scientific studies devoted to preventing

the occurrence and progression of LSIL, the prevalence of cervical cancer has not decreased, necessitating further research in this area.

Objective of the study: To improve the management of reproductive-age patients with persistent human papillomavirus types 16 and/or 18, taking into account the results of clinical, anamnestic, and colposcopic examination methods.

Material and methods.

This study presents the results of a prospective study conducted at the Abu Ali Ibn Sina Bukhara State Medical Institute from 2024 to 2025. The study included 155 women who were newly diagnosed with cervical pathology. The study aimed to identify significant clinical, anamnestic, colposcopic, and microbiological risk factors for the development of precancerous cervical lesions. Next, 2 groups were formed based on the results of cytological examination, taking into account the inclusion/exclusion/removal criteria: Group 1 (main group) - patients with HSIL based on the results of cytological examination, confirmed by histological examination (n=45); Group 2 (comparison) – patients with NILM based on histologically confirmed cytology and an abnormal colposcopic picture, n=30. Inclusion criteria for the main and comparison groups: HSIL based on histologically confirmed cytology or NILM based on histologically confirmed cytology and an abnormal colposcopic picture; age 18-49 years; persistence of HPV types 16 and/or 18 for more than 24 months; no HPV vaccination; transformation zone type 1 or 2 based on colposcopy; microscopic vaginal discharge corresponding to normocenosis or intermediate type; signed informed consent for the study. Exclusion criteria: patients who received antibiotics within 15 days prior to sample collection; patients who had sexual intercourse or douching within 48 hours prior to sample collection. Exclusion criteria: NILM based on cytological examination results in the presence of a normal colposcopic picture; ASCUS based on cytological examination results; absence of HPV; presence of HPV HCR other than types 16 and 18.

Results of the study

In accordance with the aim of our work and the established objectives, a comparative analysis was conducted between the groups taking into account clinical, anamnestic, and colposcopic data. In the main group, the median age was 36.00 (28.50; 40.50) years, in the comparison group, the average age was 34.40 (6.044) years. The groups were comparable in the presence of somatic and gynecological diseases. Among the concomitant diseases, ENT pathology was the most common in patients of both groups. In the main group, it amounted to 22.2%, in the comparison group - 26.7%. Among the gynecological diseases in the anamnesis, cervical ectopy was the most common in patients of the main group (44.4%), and in women of the comparison group - 33.3%. No statistically significant differences were found in education level, working conditions, alcohol consumption, menstrual function, contraception use, number of pregnancies and their outcomes, pregnancy and childbirth complications, or unprotected sex. Tobacco use was found to increase the risk of developing HSIL by 4.4 times ($p=0.007$).

Unprotected sex was found to increase the risk of developing HSIL by 6.8 times ($p<0.001$). When assessing the body mass index (BMI) by group, the average BMI in the study group was 25.40, while in the comparison group it was 23.95 ($p=0.027$). Women in the study group had an average of 4 partners, while in the comparison group it was 2 ($p=0.001$). The age of sexual debut was 16 years in the study group, while in the comparison group it was 18 ($p=0.004$). When analyzing the data of extended colposcopy, statistically significant differences were found between the groups for the following characteristics: the odds of having grade 1 ACC were 10.7 times higher in the comparison group compared to the main group ($p<0.001$). The probability of having thin acetowhite epithelium with an uneven contour in the main group was 3.1 times higher than in the comparison group ($p=0.018$). The chances of having the "rapid whitening" feature in the main group were 5.2 times higher than in the comparison group ($p=0.005$). The probability of having dense acetowhite epithelium with a clear contour in the main group was 17.6 times higher than in the comparison group ($p<0.001$). The chances of detecting a dense acetowhite rim around open glands were 10.2 times higher in the main group than in the comparison group ($p<0.001$). No statistically significant differences were found for the remaining parameters. During the examination of women in the main group, HPV type 16 was detected in 41

patients, HPV type 18 in 14. Both types were found in 10. In the comparison group, HPV type 16 was found in 22 women, HPV type 18 in 12, and both types in 4.

Women with persistent HPV types 16 and/or 18, NILM, and abnormal colposcopic findings are asked, in addition to a routine examination, to answer the following questions: age at first sexual activity, number of sexual partners, and history of unprotected intercourse. An obstetrician-gynecologist interprets the colposcopy results, focusing on the presence of acetowhite epithelium around the exposed glands. To verify the diagnosis, a cervical biopsy is collected, sent for histological examination, and sent to a microbiology laboratory to detect *Streptococcus* spp. These factors are predictors of the development of HSIL. All women are recommended conservative therapy, correction of dysbiosis based on the isolated cervical microbiota, and recommendations for eliminating significant risk factors. If the P value is greater than or equal to 0.624, HPV testing and cytological examination should be performed after 3-6-12 months; if the P value is less than 0.624, HPV testing and cytological examination should be performed after 12 months.

Conclusions

1. The presence of reliable risk factors (smoking, high body mass index, early sexual debut, a large number of sexual partners, and unprotected sex) allows us to identify a group of patients at risk for severe intraepithelial lesions among women with persistent HPV types 16 and/or 18, no intraepithelial lesions based on cytological examination, and abnormal colposcopic findings.
2. The most significant colposcopic features were identified in patients with HSIL and persistent HPV types 16 and/or 18.

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