

## RISK FACTORS OF PRE-CANCER CERVICAL DISEASES IN WOMEN OF REPRODUCTIVE AGE

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**Relevance.** Today, the nature of the impact of the inflammatory process caused by *Trichomonas infection* on the persistence of HPV and immune response, as a consequence of the progression of intraepithelial lesions of the cervix, is not fully understood.

**Objectives:** based on a retrospective clinical and statistical analysis to determine the risk factors for cervical dysplasia in women of reproductive age.

**Materials and methods.** A clinical and statistical analysis for 392 medical records of patients of reproductive age with verified HPV and *Trichomonas Vaginalis*, who received pathogenetic therapy at the clinical bases of the Bogomolets National Medical University Obstetrics and Gynecology № 3 Department and LLC “Clinic Profimed” for 2015-2019. As a result of a retrospective study of patients systematized by age, complaints, the presence of genital and extragenital pathology, reproductive history and the state of reproductive function, social status.

**Results.** According to the analysis of anamnesis indicators, the main risk factors for precancerous cervical conditions were: early onset of sexual life, menstrual disorders (29.1%), high incidence of childhood infectious diseases (63.5%), somatic pathology (71.2 %), irregular use of barrier contraception (19.9%), genital diseases caused by sexually transmitted infections (STD), including HPV and *Trichomonas Vaginalis*, frequent abortions (41.6%) and childbirth with cervical trauma, low level of medical and sexual cultures and smoking (65.3%). The systemic negative impact of numerous risk factors on the body contributed to cervical intraepithelial neoplasia (CIN) development in women of reproductive age.

**Conclusion.** The retrospective study proves the need for stratification of patients with for CIN risk, requires management of cervical pathology in women with HPV and detected *Trichomonas Vaginalis*, which will increase the effectiveness of diagnosis, treatment and recurrence prevention.

**Keywords:** cervical dysplasia, chronic cervicitis, human papilloma virus, *Trichomonas Vaginalis*.

**Relevance.** Cervical diseases associated with human papillomavirus (HPV) are a problem of modern obstetrics and gynecology, especially the review of pandemic spread of the pathogen in the population of women of reproductive age and the possibility of precancerous processes and cervical cancer [3, 4]. The strategy of secondary prevention of cervical cancer is early detection of benign HPV-associated cervical diseases. About 79 million people are infected with HPV worldwide. In turn, the frequency of HPV in chronic cervicitis (HC) is 14.5-86% [5, 7]. Also, not excluded the possibility of developing precancer and cervical cancer in patients with HC on the background of *Trichomonas infection* in conditions of persistent HPV infection [2, 11].

According to experts from the IARC (International Agency for Research on Cancer), despite the fact that cervical cancer is a malignant neoplasm of visualized localization, in 2020 the number of first detected cases in the world will increase by almost 40% [4, 9]. The early detection and treatment of precancerous conditions of the cervix are effective in cervical cancer prevention.

Management tactic and treatment of women of reproductive age in case of of cervical dysplasia (CIN) detection and *Trichomonas infection* are quite different: “wait-and-see” strategy with the use of HPV testing and cytological control, microscopy and cultural method, polymerase chain reaction (PCR) and lateral flow method usage, excision (sometimes repeated) and even – hysterectomy [1, 8, 10]. Deserve particular attention the tactics of women with CIN the opportunity to residual&recurrence of disease [6, 9].

However, in the pathogenesis of cervical dysplasia, the dependence of high-oncogenic HPV types activity, in cause of CIN development on the nature of the inflammatory process of the cervix, remains insufficiently studied. With the background of the inflammatory process is the penetration of papillomavirus into the basal level with subsequent violation of the stratification of the multilayer epithelium of the cervix. The subject of discussion is the nature of the impact of the inflammatory process caused by *Trichomonas infection* on the persistence of HPV and immune response, as a consequence of the progression of intraepithelial lesions of the cervix.

**Objectives:** based on a retrospective clinical and statistical analysis to determine the risk factors for cervical dysplasia in women of reproductive age.

### MATERIALS AND METHODS

The study was conducted at the clinical bases of the Bogomolets National Medical University Department of Obstetrics and Gynecology № 3 and LLC “Clinic Profimed” in 2015-2019, which included clinical and statistical analysis of archival material of 392 medical cards of outpatients (№025 / o) with chronic cervicitis / cervical intraepithelial neoplasia, treated with different methods and schemes. Inclusion criteria in the retrospective study were: reproductive age, the presence of HPV with the result of the PAP-test ASCUS, LSIL, HSIL, detected *Trichomonas Vaginalis*. Exclusion criteria: age under 18 and over 45 years, the presence of malignancy on the basis of histological examination, pregnancy or lactation, mental disorders.

As a result of the analysis of medical records, we systematized the age categories of patients, the nature of complaints, reproductive history, generative function, the presence of genital and extragenital pathology, social status.

### RESULTS AND DISCUSSION

In a retrospective study, it was found that the average age was  $32.3 \pm 1.2$  years. Conducted analysis of the age distribution of patients revealed the predominance of age categories “25-29” and “30-34 years” (Fig. 1). 297 (75.8%) respondents from HC / CIN lived in Kyiv and 95 (24.2%) in Kyiv oblast. 392 of the women who took part in the retrospective study: 136 (34.7%) did not work, 229 (58.4%) belonged to the category of employees, 27 (6.9%) - worked in industrial production.

The analysis of marital status showed that there were 165 (42.1%) women in a registered marriage, 74 (18.9%) were officially divorced, 153 (39.0%) were out of wedlock, but had sex. Due to the lack of information in the medical cards, it was not possible to assess sexual behavior. The mean age of sexual activity onset in women with HC / CIN was  $17.8 \pm 0.2$  years.

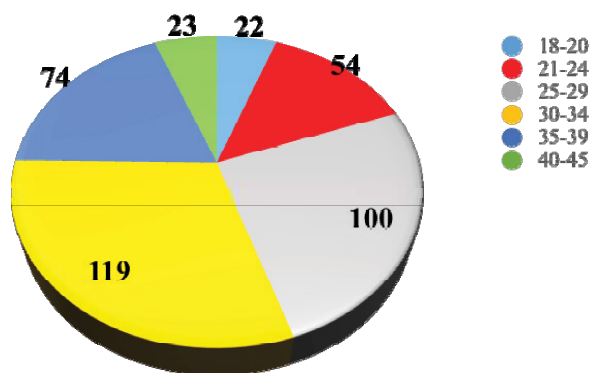


Fig. 1. Age categories of women (abs.)

Among retrospectively surveyed women, 256 (65.3%) indicated smoking and 125 (31.9%) alcohol consumption. However, it was not possible to determine the intensity of smoking and the nature of the alcohol consumption in the medical documentation.

Analysis of anthropometric parameters in women with HC / CIN did not reveal growth and weight characteristics, the average body mass index was 27.2 kg / m<sup>2</sup>.

Concomitant extragenital pathology is of fundamental importance in women with HC / CIN, which was found in 279 (71.2%) women, a combination of several diseases was noted in 137 (34.9%) patients (Fig. 2).

Gastrointestinal diseases were found in 187 (47.7%) respondents, among whom the most common were chronic gastritis, biliary dyskinesia, peptic ulcer disease, cholecystitis and pancreatitis.

Pediatric infectious diseases occurred in 249 (63.5%) patients. We did not perform a structural analysis of the presented pathology due to the lack of information in the medical records.

Endocrine pathology were observed in 159 (40.6%) patients with obesity, pathological conditions of the thyroid gland, diabetes mellitus.

Pathology of the urinary system occurred in 136 (34.7%) women, in its structure consisted of chronic pyelonephritis, cystitis, urolithiasis.

Respiratory system disease was noted in 113 (28.8%) patients with a history of chronic bronchitis and bronchial asthma. Of the pathological conditions of the ENT organs, diagnosed in 100 (25.5%) women, chronic tonsillitis prevailed.

Allergic anamnesis was burdened with household allergies, allergic reactions to drugs, pollinosis in 23 (5.9%) women.

Pathology of the cardiovascular system was found in 16 (4.1%) women with predominant neurocirculatory dystonia. Veins varicose were diagnosed in 91 (23.2%) retrospectively examined women, which in almost all cases is represented by pathological changes in the vessels of the lower limbs.

Menstruation in the majority of patients began on time, at 11-14 years, the average age of menarche according to medical records was  $12.6 \pm 1.4$  years. Analysis of menstrual function revealed that 114 (29.1%) patients had dysmenorrhea, 62 (15.8%) had premenstrual syndrome.

Retrospective analysis of gynecological morbidity in examined women with HC / CIN in the anamnesis of 126 (32.1%) respondents revealed chronic salpingo-oophoritis, in 45 (11.5%) – benign ovarian tumors. Among gynecological pathology in 42 (10.7%) women diagnosed intrauterine pathology in 56 cases (14.3%). Primary or secondary infertility occurred in almost one in five cases (19.1%).

High frequency of genital inflammatory processes caused by sexually transmitted infections deserves particular attention. 155 (39.5%) women had a history of vaginitis and cervicitis, and 41 (10.5%) had

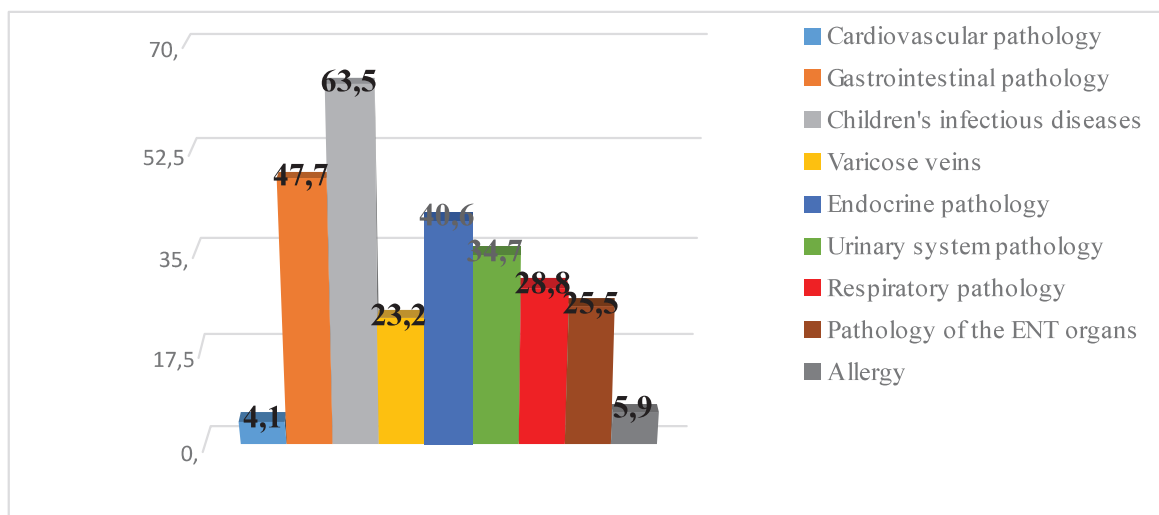


Fig. 2. Extragenital pathology in retrospectively examined women (%)

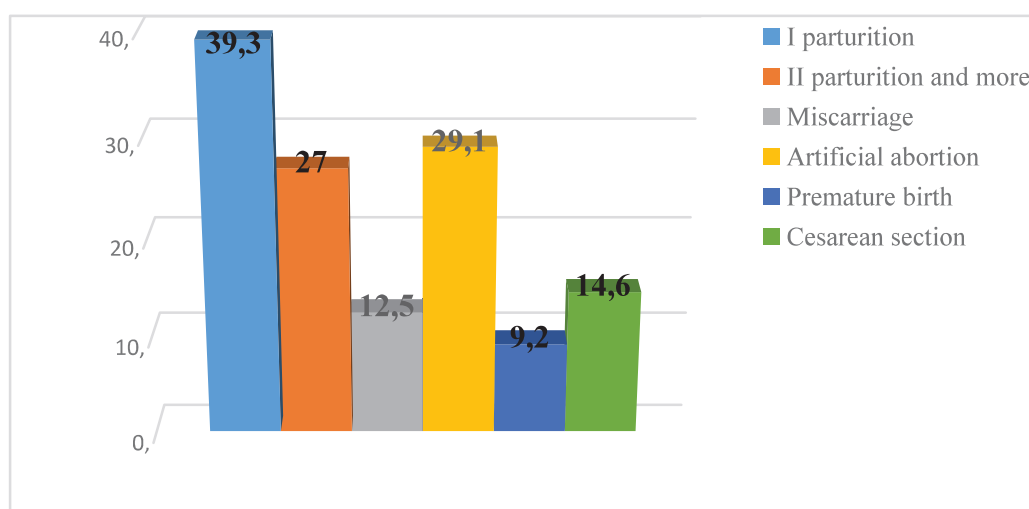


Fig. 3. Reproductive history of retrospectively examined women

hydrosalpinx / sactosalpinx. Anamnestic dysbiosis of the vaginal biotope was detected in 243 (62.0%), chlamydial urogenital infection in 48 (12.2%), mycoplasma – in 37 (9.4%), ureaplasma – in 45 (11.5%), herpes virus infection - in 54 (13.8%) patients with HC / CIN.

Surgical interventions on the pelvic organs, according to the presented medical records, were performed in 59 (15.1%) retrospectively examined patients. In 16 (4.1%) cases cystectomy was performed, in 26 (6.6%) – ectopic pregnancy surgery, 11 (2.8%) – selective myomectomy. Destructive treatment of the cervix for intraepithelial cervical neoplasia performed 54 (13 , 8%) patients. Among the methods of destructive treatment in 10 (18.5%) cryodestruction was used, in 25 (46.3%) – radiowave excision, in 19 (35.2%) – diathermalelectroexcision of the cervix.

A retrospective study of the reproductive function of women with cervical neoplasia (Fig. 3), which took into account the onset of sexual activity and the consequences

of pregnancy found in the anamnesis of 154 (39.3%) respondents one childbirth, 106 (27%) gave birth twice or more, 49 (12.5%) of pregnant women had miscarriage, 76 (19.4%) women had no pregnancy. 114 (29.1%) responded woman made artificial abortions. The 49 women who had a history of miscarriage: 41 (83.7%) had it in the first trimester, and 8 (16.3%) had a late miscarriage. One miscarriage was noted in the anamnesis – 33 (8.4%) of women, two – 10 (2.6%), three or more – 6 (1.5%) retrospectively examined women. Cases of premature birth were reported in 24 (9.2%) women. 38 (14.6%) patients had a history of cesarean section. The causes of miscarriages and premature births could not be determined due to the lack of data in medical cards.

For the purpose of contraception 81 (20.7%) women used physiological (calendar) method, 62 (15.9%) – hormonal and 78 (19.9%) barrier methods, 20 (5.1%) IUD, however 151 (38.5%) patients did not prevent unwanted pregnancies at all.

Retrospectively was found that the main risk factors for precancerous conditions of the cervix are early sexual life, low level of medical and sexual culture, the presence of sexually transmitted infections, frequent abortions and childbirth. In most patients there is a combination of several risk factors. Direct interaction between risk factors and their systemic effects on the body may create the preconditions for the development of cervical neoplasia in women of reproductive age.

This category of patients revealed a significant prevalence of smoking, menstrual disorders, high rates of childhood infectious diseases, pathology of the gastrointestinal tract, urinary system and ENT diseases, irregular use of barrier contraception, a significant frequency of inflammatory processes of the genitals caused by infections. Sexually transmitted diseases, including HPV and *Trichomonas Vaginalis* were present. According to the results of a retrospective study, risk factors for cervical neoplasia include increased trauma to the cervix due to artificial abortions and medical manipulations that accompany miscarriages.

Our retrospective study proves the need for stratification of patients at risk for cervical intraepithelial neoplasia, requires management of cervical pathology in women with CIN due to STIs, which will improve the diagnosis and treatment results, as well as prevent the development of recurrence.

## CONCLUSION

Based on a retrospective analysis, was found that the factors of precancerous conditions of the cervix should be defined as: early sexual life, menstrual irregularities (29.1%), high incidence of childhood infectious diseases (63.5%), somatic pathology (71.2%), irregular use of barrier contraception (19.9%), genital inflammatory diseases caused by sexually transmitted infections, including HPV and *Trichomonas Vaginalis*, frequent abortions (41.6%) and childbirth with cervical trauma, low level of medical and sexual culture, smoking (65.3%). Systemic adverse effects of numerous risk factors on the body contributed the development of CIN in women of reproductive age.

Конфлікт інтересів: відсутній.  
Conflicts of interest: authors have no conflict of interest to declare.  
Надійшла до редакції / Received: 10.01.2020  
Після доопрацювання / Revised: 13.01.2020  
Прийнято до друку / Accepted: 28.02.2020

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## ФАКТОРИ РИЗИКУ ВИНИКНЕННЯ ПЕРЕДРАКОВИХ ЗАХВОРЮВАНЬ ШИЙКИ МАТКИ У ЖІНОК РЕПРОДУКТИВНОГО ВІКУ

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**Актуальність.** Сьогодні не до кінця вивчений характер впливу запального процесу, викликаного трихомонадною інфекцією, на персистенцію вірусу папіломи людини (ВПЛ) і імунну відповідь, як наслідок прогресування внутрішньоепітеліальних поразок шийки матки.

**Мета:** на основі проведення ретроспективного клініко-статистичного аналізу визначити фактори ризику виникнення дисплазії шийки матки у жінок репродуктивного віку.

**Матеріали та методи.** Проведено клініко-статистичний аналіз 392 карт амбулаторних хворих репродуктивного віку з верифікованими ВПЛ та *Trichomonas Vaginalis*, що отримували патогенетичну терапію на клінічних базах кафедри акушерства і гінекології № 3 Національного медичного університету імені О.О. Богомольця та ТОВ «Клініка Профімед» за 2015-2019 р.р. В результаті ретроспективного дослідження пацієнток систематизовано за віковими категоріями, характером скарг, наявністю генітальної та екстрагенітальної патології, репродуктивним анамнезом і станом генеративної функції, соціальним статусом.

**Результати.** За аналізом анамнестичних показників визначено основні чинники ризику виникнення передракових станів шийки матки, а саме: ранній початок статевого життя, порушення менструального циклу (29,1%), висока частота дитячих інфекційних захворювань (63,5%), соматичної патології (71,2%), нерегулярне використання бар'єрної контрацепції (19,9%), запальних захворювань геніталій, викликаних інфекціями, що передаються статевим шляхом, зокрема ВПЛ та *Trichomonas Vaginalis*, часті аборти (41,6%) та пологи з травматизацією шийки матки, низький рівень медичної та сексуальної культури, табакопаління (65,3%). Системний негативний вплив численних факторів ризику на організм сприяв розвитку неоплазій шийки матки у жінок репродуктивного віку.

**Висновки.** Проведене ретроспективне дослідження доводить необхідність стратифікації пацієнток груп ризику щодо виникнення цервікальної інтраепітеліальної неоплазії, потребує менеджменту патології шийки матки у жінок з наявністю ВПЛ та виявленою *Trichomonas Vaginalis*, що сприятиме підвищенню ефективності діагностики, лікування та попередженню розвитку рецидивів дисплазій епітелію шийки матки у жінок репродуктивного віку.

**Ключові слова:** дисплазія шийки матки, хронічний цервіцит, вірус папіломи людини, *Trichomonas Vaginalis*.

## ФАКТОРЫ РИСКА ВОЗНИКНОВЕНИЯ ПРЕДРАКОВЫХ ЗАБОЛЕВАНИЙ ШЕЙКИ МАТКИ У ЖЕНЩИН РЕПРОДУКТИВНОГО ВОЗРАСТА

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**Актуальность.** Сегодня не до конца изучен характер влияния воспалительного процесса, вызванного трихомонадной инфекцией, на персистенцию вируса папилломы человека (ВПЧ) и иммунный ответ, как следствие прогрессирования внутриэпителиальных поражений шейки матки.

**Цель:** на основании проведенного ретроспективного клинико-статистического анализа определить факторы риска возникновения дисплазии шейки матки у женщин репродуктивного возраста.

**Материалы и методы.** Проведен клинико-статистический анализ 392 карт амбулаторных больных репродуктивного возраста с верифицированными ВПЧ и *Trichomonas Vaginalis*, которые получали патогенетическую терапию на клинических базах кафедры акушерства и гинекологии № 3 Национального медицинского университета имени А.А. Богомольца и ООО «Клиника Профимед» за 2015-2019 г.г. В результате ретроспективного исследования пациентки систематизированы по возрастным категориям, характеру жалоб, наличию генитальной и экстрагенитальной патологии, репродуктивному анамнезу и состоянию генеративной функции, социальному статусу.

**Результаты.** Анализ анамнестических показателей выявил основные факторы риска возникновения предраковых состояний шейки матки, а именно: раннее начало половой жизни, нарушения менструального цикла (29,1%), высокую частоту детских инфекционных заболеваний (63,5%), соматической патологии (71,2%), нерегулярное использование барьерной контрацепции (19,9%), воспалительные заболевания гениталий, вызванные инфекциями, передающимися половым путем, в том числе ВПЧ и *Trichomonas Vaginalis*, а также частые абORTы (41,6%) и роды с травматизацией шейки матки, низкий уровень медицинской и сексуальной культуры, табакокурение (65,3%). Системное неблагоприятное влияние многочисленных факторов риска способствовало развитию неоплазий шейки матки у женщин репродуктивного возраста.

**Выводы.** Проведенное ретроспективное исследование доказывает необходимость стратификации пациенток групп риска по возникновению цервикальной интраэпителиальной неоплазии, менеджмента патологии шейки матки у женщин с наличием ВПЧ и выявленной *Trichomonas Vaginalis* для повышения эффективности диагностики, лечения и предупреждения рецидивирования дисплазий эпителия шейки матки у женщин репродуктивного возраста.

**Ключевые слова:** дисплазия шейки матки, хронический цервицит, вирус папилломы человека, *Trichomonas Vaginalis*.