INTERNATIONAL JOURNAL OF
INTEGRATIVE AND
MODERN MEDICINE

# Influence of Hormonal and Intrauterine Contraceptive Methods on Cervical Health and Hpv-Related Changes

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**Abstract:** Cervical cancer remains one of the most common malignancies among women worldwide. Persistent infection with high-risk human papillomavirus (hrHPV) types is the primary etiological factor. Despite the effectiveness of HPV vaccination and cervical screening, the burden of disease remains high, particularly in low- and middle-income countries. The influence of contraceptive methods—especially combined oral contraceptives (COCs) and intrauterine devices (IUDs)—on cervical epithelial health and HPV-related pathology continues to be debated. This study is conducted to evaluate the potential relationship between the use of COCs and IUDs and the occurrence of cervical epithelial and microbiological alterations, including inflammatory and dysplastic changes, in women of reproductive age.

**Key words:** Cervical dysplasia; HPV infection; intrauterine device (IUD); combined oral contraceptives (COC); cervical screening; Pap test; colposcopy; vaginal microbiota; reproductive health

## INTRODUCTION

Cervical cancer remains one of the leading causes of cancer among women worldwide. According to the World Health Organization (WHO), in 2020, there were approximately 604,000 new cases and 342,000 deaths from the disease [17]. Oncogenic strains of human papillomavirus (hrHPV) — also known as high-risk types, including types 16, 18, 31, 33, 35, 45, 52, and 58 — are a necessary but not sufficient cause of cervical cancer [4]. The risk of developing cervical cancer can be reduced through vaccination against hrHPV types and/or screening for early detection and treatment of cervical dysplasia [5]. However, not all women undergo vaccination or screening. Although these preventive measures are effective, health education and awareness campaigns can be difficult to implement in settings with weak healthcare systems, particularly in low- and middle-income countries [13]. Understanding the risk-modifying factors that promote the progression of HPV infection to cervical dysplasia and/or cancer could help design targeted interventions to increase vaccination and screening coverage.

According to the United Nations Population Division (2023), the global use of modern contraceptive methods continues to rise, with intrauterine devices (IUDs) and combined oral contraceptives (COCs) remaining among the most widely used forms of birth control worldwide [16]. One of the proposed risk factors for HPV progression to cervical dysplasia or cancer is the use of combined oral contraceptives (COCs) [8,12]. The International Agency for Research on Cancer (IARC) has classified COCs as a causal factor for cervical cancer [9]. A meta-analysis conducted in 2007 by the International Collaboration of Epidemiological Studies of Cervical Cancer, which included individual data from 24 epidemiological studies, demonstrated that among current oral contraceptive (OC) users, the risk of invasive cervical cancer increases with duration of use [3]. This finding suggests that OCs may enhance HPV-induced carcinogenesis. However, it remains unclear to what extent these results are influenced by confounding factors such as sexual behavior, lifestyle, and frequency of screening [10]. Moreover, these studies did not distinguish between COCs and progestin-only pills [3, 8], and the

impact of other hormonal contraceptive methods on the risk of HPV progression to dysplasia or cervical cancer also remains uncertain.

While previous studies have demonstrated a possible association between hormonal contraceptive use and the risk of cervical cancer, the evidence regarding the use of intrauterine devices (IUDs) remains contradictory [1, 2, 6, 7, 10, 39]. A pooled analysis of 26 epidemiological studies conducted by Castellsagué et al. even suggested that IUD use may act as a protective factor against cervical cancer [6]. Recent large-scale cohort studies from Denmark and South Korea have explored the potential association between contraceptive use—particularly IUDs and hormonal methods—and the risk of cervical intraepithelial neoplasia and HPV infection, yielding mixed results regarding their protective or predisposing effects on cervical pathology [11, 15].

## MATERIALS AND METHODS

This prospective study was conducted at the Women's Health Center of the Tashkent Medical Academy and included data from 107 women of reproductive age, collected between November 2023 and September 2024.

The participants were divided into three groups:

- Group I (Control group) — 40 women who did not use combined oral contraceptives (COCs) or intrauterine devices (IUDs);
- Group II (COC group) — 31 women using combined oral contraceptives;
- Group III (IUD group) — 34 women using intrauterine devices.

Exclusion criteria included: pregnancy at the time of the study, absence of childbirth in the medical history, exclusively operative delivery, presence of harmful habits, increased body mass index, presence of sexually transmitted infections, age under 20 or over 49 years, and incomplete medical records.

Comprehensive examination included the following methods:

- Clinical examination, involving history taking and physical assessment;
- Gynecological examination, including visual inspection of the external genitalia, examination of the vagina and cervix using specula, and bimanual palpation;
- Laboratory tests: complete blood count (CBC), vaginal smear microscopy, bacteriological culture with antibiotic sensitivity testing, and polymerase chain reaction (PCR) for detection of human papillomavirus (HPV);
- Cytological examination of the cervix using the Papanicolaou (Pap) test;
- Colposcopy, assessing the cervical epithelium and transformation zone.

For data processing and statistical analysis, descriptive and comparative statistical methods were applied. Mean values, standard deviations, and standard errors of the mean were calculated. The Student's t-test was used to assess the statistical significance of intergroup differences, with a p-value $< 0.05$ considered statistically significant.

## RESULTS

### *A. Clinical Examination*

Analysis of the age composition of the study participants across all three groups showed that all women were within the reproductive age range — from 20 to 49 years.

The mean age of patients was $38.3 \pm 0.8$ years in the control group, $38.4 \pm 1.2$ years among women using combined oral contraceptives (COCs), and $37 \pm 1.3$ years in the intrauterine device (IUD) group, indicating no statistically significant differences between the groups for this parameter.

The mean age at menarche was comparable across all groups: 13.4 ± 0.6 years in the control group, 13.4 ± 0.2 years among COC users, and 13.4 ± 0.2 years among IUD users.

The distribution by age categories showed that the largest proportion of women experienced menarche at 13 years (32.5%, 35.5%, and 32.3%, respectively).

Assessment of menstrual function revealed that most women maintained regular menstrual cycles, although their frequency varied among groups: 77.5% in the control group, 55.0% among COC users, and 85.3% among IUD users.

Consequently, irregular menstruation was more frequently observed in women using hormonal contraception (22.5% in the control group, 29.0% in the COC group, and 14.7% in the IUD group).

Analysis of menstrual disorders showed that polymenorrhea was more common among IUD users (20.6%) compared with the control (5.0%) and COC groups (9.7%).

Conversely, oligomenorrhea occurred in 5.0% of the control group and 12.9% of COC users, while it was not observed among IUD users.

Dysmenorrhea was a relatively frequent symptom, reported by 22.6% of women in the control group, 29.0% of COC users, and 32.3% of IUD users (Table 1).

***Table 1.*** **Characteristics of the menstrual cycle among the study participants (abs., %)**

| **Menstrual characteristics** | I group(n=40) | II group(n=31) | III group(n=34) |
|---|---|---|---|
| ***Regular*** | 31(77,5%) | 22(55%) | 29(85,3%) |
| ***Irregular*** | 9(22,5%) | 9(29%) | 5(14,7%) |
| ***Polymenorrhea*** | 2(5%) | 3(9,7%) | 7(20,6%) |
| ***Oligomenorrhea*** | 2(5%) | 4(12,9%) | 0(0%) |
| ***Dismenorrhea*** | 7(22,6%) | 9(29%) | 11(32,3%) |

Pregnancies

Analysis of reproductive history showed that the majority of women had between one and five pregnancies. Specifically, 1–3 pregnancies were reported in 47.5% of women in the control group, 38.7% of COC users, and 52.9% of IUD users.

Four to five pregnancies occurred in 27.5%, 41.9%, and 26.5% of women in the respective groups. More than five pregnancies were relatively uncommon, observed in 25.0% of the control group, 16.1% of COC users, and 20.6% of women in the IUD group. Thus, the highest frequency of multiple pregnancies (>4) was recorded among women in the control group.

***Deliveries***

The majority of women across all three groups had 1–3 deliveries: 75.0% in the control group, 83.9% among COC users, and 76.5% among IUD users.

Four to five deliveries were recorded in 15.0%, 16.1%, and 20.6% of women, respectively. Cases of more than five deliveries were rare and observed only in the IUD group (2.9%). Overall, reproductive activity was comparable across groups, although women in the control group were slightly more likely to have ≥4 deliveries.

***Cervical Trauma***

A history of cervical tears was found in 20.0% of women using COCs, 12.9% of IUD users, and 17.6% of women in the control group.

The vast majority of participants had no history of cervical trauma (80.0%, 87.1%, and 82.4%, respectively).

### *Miscarriages*

The frequency of spontaneous miscarriages was generally moderate across all groups. A single miscarriage was reported in 17.5% of women in the control group, 16.1% of COC users, and 20.6% of IUD users.

Two miscarriages were less common — observed in 2.5% of the control group and 5.9% of IUD users, while no such cases occurred among COC users.

The most severe cases (three spontaneous miscarriages) were recorded only among 5.0% of women in the control group and were absent in the other two groups.

### *Induced Abortions*

Induced abortions were relatively frequent among the study participants.

A single abortion was most common, reported in 37.5% of women in the control group, 19.3% of COC users, and 20.6% of IUD users.

Two abortions occurred in 12.5%, 16.1%, and 11.7%, respectively.

Three abortions were recorded in 7.5% of the control group, 9.7% of COC users, and 8.8% of IUD users. Four abortions were observed primarily in the control group (5.0%) and less frequently among COC users (3.2%), while no such cases were reported in the IUD group. Overall, the highest cumulative frequency of abortions was observed among women using COCs, possibly reflecting differences in reproductive history and contraceptive adherence.

### *B. Gynecological Examination*

Comparative analysis of speculum examination data among the three study groups revealed that the frequency of visual cervical and vaginal changes varied depending on the method of contraception used. The largest proportion of women without pathological changes of the cervix and vagina was observed in the control group (37.5%) and among IUD users (41.2%). Among women using combined oral contraceptives (COCs), this rate was slightly lower (35.3%), reflecting a trend toward a higher frequency of detectable morphological alterations in this category.

The distribution of specific morphological changes differed across groups.

Cervical hypertrophy and endocervical polyps were found in similar proportions in all groups, showing no significant intergroup variation. Cervical scarring was more frequently observed in the control group (20%), whereas among COC users (12.9%) and IUD users (17.6%), its occurrence was somewhat lower. Particular attention should be given to cervical ectopy, which was most frequent among IUD users (29.4%), compared with 20% in the control group and 16.1% in the COC group. A similar trend was noted for vulvovaginal papillomas, which were detected in 20.6% of IUD users—substantially higher than in the control group (7.5%) and COC users (6.5%). Condylomas were relatively uncommon, occurring mainly in the control (7.5%) and IUD (5.9%) groups, with only isolated cases among COC users (3.2%).

Nabothian cysts were also more frequently observed among IUD users (17.6%), compared with 7.5% in the control group and 12.9% among COC users. Contact bleeding occurred with a similar frequency across all groups (9.7–12.5%), without statistically significant differences.

In summary, the most notable differences were related to the higher incidence of cervical ectopy and vulvovaginal papillomas among women using IUDs, which may reflect the local tissue effects of intrauterine contraception and potentially contribute to viral infection persistence (Table 2).

**Table 2. Gynecological findings during speculum examination (abs., %)**

| Visual characteristics | I group(n=40) | II group(n=31) | III group(n=34) |
|---|---|---|---|
| ***No visual changes*** | 15(37,5%) | 12(35,3%) | 14(41,2%) |
| ***Cervical hypertrophy*** | 3(7,5%) | 2(6,5%) | 3(8,8%) |
| ***Cervical rupture*** | 8(20%) | 4(12,9%) | 6(17,6%) |
| ***Cervical ectopy*** | 8(20%) | 5(16,1%) | 10(29,4%) |
| ***Endocervical polyp*** | 5(12,5%) | 3(9,7%) | 3(8,8%) |
| ***Vulvovaginal papilloma*** | 3(7,5%) | 2(6,5%) | 7(20,6%) |
| ***Condyloma*** | 3(7,5%) | 1(3,2%) | 2(5,9%) |
| ***Nabothian cysts*** | 3(7,5%) | 4(12,9%) | 6(17,6%) |
| ***Contact bleeding*** | 5(12,5%) | 3(9,7%) | 4(11,7%) |

**C. Bacteriological Examination**

Bacteriological analysis of vaginal specimens from women in the three study groups revealed differences in the spectrum of isolated microorganisms. In the control group (n = 40), the vaginal microflora was predominantly normal: conditionally pathogenic microorganisms were identified in 4 women (10%), and obligate pathogenic bacteria in 4 women (10%). Mixed infections were observed in 3 cases (7.5%), while fungal flora was not detected in this group.

Among women using combined oral contraceptives (COCs) (Group II, n = 31), the microbial pattern differed slightly. Conditionally pathogenic flora was not detected, whereas both obligate pathogens and mixed infections were more common than in the control group — 5 cases each (16.1%). Fungal flora was found in one case (3.2%).

In the group of IUD users (Group III, n = 34), a similar trend toward a higher frequency of pathogenic microorganisms was observed compared to the control group.

Conditionally pathogenic bacteria were detected in 2 women (5.9%), and obligate pathogens in 4 (11.8%). Fungal flora was identified in one case (2.9%), and mixed infections were present in 5 women (14.7%), exceeding the rate observed in the control group (Table 8). Overall, the findings suggest a greater prevalence of mixed and pathogenic microbial colonization among women using hormonal and intrauterine contraceptives, particularly in the IUD group, indicating a possible influence of contraceptive methods on vaginal microbiocenosis stability (Table 3).

**Table 3. Bacteriological findings in vaginal smears of study participants (abs., %)**

| | I group(n=40) | II group(n=31) | III group(n=34) |
|---|---|---|---|
| ***Opportunistic flora*** | 4(10%) | 0(0%) | 2(5,9%) |
| ***Obligate-pathogenic flora*** | 4(10%) | 5(16,1%) | 4(11,8%) |
| ***Fungal flora*** | 0(0%) | 1(3,2%) | 1(2,9%) |
| ***Mixed infections*** | 3(7,5%) | 5(16,1%) | 5(14,7%) |

***D. Cytological Examination***

Cytological examination of cervical smears revealed that the highest proportion of normal cytograms without pathological changes was observed in the control group (57.5%), while this rate was lower among women using combined oral contraceptives (COCs) (41.9%) and lowest among intrauterine device (IUD) users (23.5%).

Inflammatory changes within NILM (Negative for Intraepithelial Lesion or Malignancy) were found predominantly among women using contraceptive methods — in 38.7% of COC users and 38.2% of IUD users, compared with only 12.5% in the control group. Atypical squamous cells of undetermined significance (ASC-US / CIN 1) were identified in 7.5% of women in the control group, 12.9% of COC

users, and 20.6% of IUD users. Low-grade squamous intraepithelial lesions (LSIL / CIN 1) were more frequently observed in the control group (22.5%), somewhat less common among IUD users (17.6%), and least frequent among COC users (6.4%) (Table 4).

**Table 4. Cytological findings among study participants (abs., %)**

| Results | I group(n=40) | II group(n=31) | III group(n=34) |
|---|---|---|---|
| ***NILM:*** | 23(57,5%) | 13(41,9%) | 8(23,5%) |
| ***NILM:inflammatory changes*** | 5(12,5%) | 12(38,7%) | 13(38,2%) |
| ***ASCUS: CIN1*** | 3(7,5%) | 4(12,9%) | 7(20,6%) |
| ***LSIL: CIN1*** | 9(22,5%) | 2(6,4%) | 6(17,6%) |

### *E. PCR Diagnostics*

Comparison of the three study groups revealed significant differences in the detection rate of high-risk human papillomavirus (HR-HPV) among women with cytological abnormalities such as ASC-US/CIN1 and LSIL/CIN1. In the control group, positive PCR results were the least frequent (33.3%). Among women using combined oral contraceptives (COCs), the prevalence of HR-HPV infection was higher (50%), indicating a trend toward increased viral detection associated with hormonal contraception.

The highest proportion of HR-HPV–positive cases was recorded among IUD users (61.5%), which was almost twice the rate observed in the control group. Thus, the highest frequency of high-risk HPV infection was found in women using intrauterine contraception, intermediate values were observed among hormonal contraceptive users, and the lowest rate occurred in the control group. These findings suggest that both hormonal and intrauterine contraceptive methods may influence local immune defenses and create conditions that favor HPV persistence.

### *F. Colposcopy*

Colposcopy was performed in 31 women with cytological abnormalities — 12 from the control group, 6 using COCs, and 13 using IUDs. Cervical dysplasia was the predominant finding in all groups (83.3%, 83.3%, and 76.9%, respectively).

Eroded ectropion and cervical scarring were more frequent among IUD users (38.4% and 30.7%), reflecting chronic irritation and previous trauma.

Papillomas were more common in COC users (33.3%) and IUD users (30.7%) than in controls (16.6%). Contact bleeding occurred mainly in the IUD group (23%), suggesting higher epithelial fragility. Nabothian cysts were found in roughly one-third of women using hormonal or intrauterine contraception. Overall, IUD users showed more inflammatory and post-traumatic cervical changes, while COC users had a slightly higher frequency of benign epithelial proliferations (Table 5).

**Table 5. Colposcopic findings among study participants (abs., %)**

| Colposcopic findings | I group(n=12) | II group(n=6) | III group(n=13) |
|---|---|---|---|
| Cervical Dysplasia | 10(83,3%) | 5(83,3%) | 10(76,9%) |
| Cervical ectropion with epithelial erosion | 3(25%) | 1(16,6%) | 5(38,4%) |
| Condyloma | 3(25%) | 1(16,6%) | 2(15,4%) |
| Papilloma | 2(16,6%) | 2(33,3%) | 4(30,7%) |
| Endocervical polyp | 2(16,6%) | 0% | 2(15,4%) |
| Contact bleeding | 1(8,3%) | 0% | 3(23%) |
| Cervical ruptures | 1(8,3%) | 1(16,6%) | 4(30,7%) |
| Cervical hypertrophy | 1(8,3%) | 0% | 0% |
| Nabothian cysts | 2(16,6%) | 2(33,3%) | 4(30,7%) |

| | | | |
|---|---|---|---|
| Post-diathermocoagulation state | 4(33,3%) | 0% | 3(23%) |

## DISCUSSIONS

The findings of this study demonstrate that both hormonal and intrauterine contraceptive methods can have measurable effects on cervical and vaginal health. Women using IUDs exhibited a higher prevalence of inflammatory and low-grade dysplastic changes, consistent with previous studies suggesting chronic mechanical irritation and localized immune modulation associated with long-term device use. The increased frequency of acetowhite epithelium, iodine-negative zones, and atypical vascular patterns among IUD users supports this hypothesis.

In contrast, COC users showed a slightly higher rate of benign epithelial proliferations and inflammatory cytological findings. This may be attributed to hormonal influences on cervical epithelial turnover and immune function. Although high-risk HPV positivity was most frequent among IUD users, the difference was not sufficient to establish causality. Rather, the observed association likely reflects a combination of behavioral, immunological, and microbiological factors.

Our results align with prior reports from the International Collaboration of Epidemiological Studies of Cervical Cancer (2007), indicating a potential increase in cervical neoplastic risk with prolonged hormonal contraceptive use, yet they also support more recent evidence suggesting that IUD use may have both adverse and protective local effects depending on duration and host response.

Notably, alterations in vaginal microbiota—including the rise in *Candida* and mixed bacterial infections—were more pronounced among IUD users. These findings emphasize the role of local dysbiosis in perpetuating chronic inflammation, which can facilitate HPV persistence and early cervical epithelial changes.

Given the multifactorial nature of cervical carcinogenesis, comprehensive preventive strategies should integrate vaccination, routine cytological and HPV screening, and careful selection of contraceptive methods, particularly for women with a history of cervical inflammation or dysplasia.

## CONCLUSIONS

1. The use of intrauterine and hormonal contraceptives was associated with an increased frequency of inflammatory and mild dysplastic cervical changes.
2. IUD users demonstrated more pronounced vaginal dysbiosis and local epithelial irritation.
3. hrHPV infection was most frequent among IUD users, suggesting possible reduced viral clearance in the presence of chronic inflammation.
4. Regular Pap testing, HPV screening, and colposcopy are essential for early detection of cervical abnormalities in contraceptive users.
5. The choice of contraceptive method should consider the patient's gynecologic history, risk factors for dysplasia, and the importance of preventive follow-up in accordance with international guidelines (WHO, FIGO, and ASCCP).

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