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## Effect of combined contraceptive pills on cervical cytology and colposcopy

Sara Hossam Ali Hussein<sup>1,\*</sup>, Amal Abd El Aziz El Said Nooh<sup>1</sup>, Amr Ahmed Abd El Rahman Esmail<sup>1</sup>, Mona Mostafa Ahmed Mohamed<sup>2</sup>, Mohamed Ahmed Mahmoud Wasfi<sup>1</sup>

<sup>1</sup> The Department of Obstetrics and Gynecology and <sup>2</sup> Pathology Department, Faculty of Medicine, Zagazig University, Zagazig, 44511 Egypt.

Corresponding author: Sara Hossam Ali Hussein

Email: [sa\\_a\\_94@yahoo.com](mailto:sa_a_94@yahoo.com)

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**Abstract: Background:** The fourth most frequent type of cancer and a major cause of death is cervical cancer. Because of its lengthy pre-invasive course, pap smears can be used as a routine screening tool to identify it.

**Aim:** utilizing the Pap test to identify cervical dysplasia and colposcopy to confirm the diagnosis, as a way of prevention and early detection of premalignant cervical cancer lesions.

**Methods:** 60 women on contraceptive pills (the combined one) undergo treatment in outpatient clinics of the hospital of Zagazig University. We perform PAP smear and colposcopic examination if there are abnormal findings to all involved patients.

**Results:** 43.3% of cases were normal, 38.3% showed inflammatory changes, and 18.3% were abnormal. Among the abnormal results, 3.3% were classified as Low-Grade Squamous Intraepithelial Lesion (LG SIL), 11.7% were identified as Atypical Squamous Cells of Undetermined Significance (ASCUS), and 3.3% showed both ASCUS and atypical endocervical glands. There's no relation between the delivery method and PAP outcomes (p-value 0.49). Parity shows no significant association with abnormal PAP (P = 0.43). Prolonged use of OCP is significantly associated with abnormal PAP (P = 0.0022)

**Conclusion:** Abnormal cytology is significantly related with long-term oral contraceptive pill use.

**Keywords:** PAP smear, Cervical Colposcope, Combined Oral Contraceptive Pills.

### Introduction

A significant amount of epidemiological evidence indicates that using oral contraceptives for an extended period of time may raise the risk of cervical cancer (1). Numerous research investigations have demonstrated a relationship between the risk factors for cervical cancer and smoking, oral contraceptive use, human papillomavirus infection, and male factor (multiple relationships) (2).

Cervical dysplasia is a premalignant lesion that may progress to cervical cancer. Cervical invasive cancer has been deemed avoidable due to its prolonged, pre-invasive phase, the availability of cervical cytology screening programs, and the efficacious treatment of pre-invasive lesions (3). Cytologic screening, or Pap smears, is the

most effective means of screening for cervical cancer. In order to obtain a sample of cells for Pap smears, the cervix must be scrapped. The cells are then sent to a lab for up to three weeks of processing and analysis (4).

A cotton bud, a tiny brush, or an Ayer's spatula a tiny wooden spatula can be used to gather the samples. An indicator of a positive test is the presence of abnormal cells, which could indicate cancer directly or chronic irritation caused by a localised yeast infection, human papilloma virus, herpes virus, or other viral infection (5). Patients who appear suspicious even with a negative pap smear or who have an abnormal pap smear result should be investigated with colposcopy and colposcopy directed biopsies (6).

Colposcopy is a non-invasive visual inspection technique that involves applying 5% acetic acid to the cervix epithelium and then taking a picture of the cervix (known as a Cervigram R 25) (7).

The objective of this work is to enable the early detection of premalignant cervical cancer lesions, identify cervical dysplasia using the Pap smear, and confirm the diagnosis with a colposcopy.

### **Patients and Methods**

The observational cross-sectional study was conducted from August 15, 2023, to February 1, 2024, at Zagazig University Hospitals, Sharkia, Egypt, in the outpatient clinic and endoscopic unit of the departments of pathology and obstetrics and gynaecology and obtained the Institutional approval.

Inclusion criteria: Patients using combined oral contraceptive pills for more than one year.

Exclusion criteria: cases with cervical cancer or dysplasia. Women using other hormonal contraceptive methods as injectable contraceptive compounds. Women who had other risk factor for cervical cancer as smokers, alcoholics and sexually promiscuous.

All cases that met the requirements for inclusion will be exposed to the following: Complete history taking, menstrual, obstetric, family, present, and past history. In the previous 24 to 48 hours, the patient is advised to avoid the following: Using a tampon, having sex, douching and putting creams or lotions on the vagina.

The vagina is then opened with a speculum. At the outpatient clinic, a cervical smear is obtained using Ayre's spatula. To obtain a sample of cells from the endocervix, the spatula is placed into the cervix's opening and rotated and a second sample is also taken from the posterior fornix and the cervix's surface (ectocervix.) Fixing the smear with 95% alcohol on a glass slide for 15 minutes. Papanicolaou stain was used to stain the slide at Zagazig University's Department of Pathology. Both basic and acidic dyes are used in the Papanicolaou stain. The basic and acidic components of the cell are stained with acidic and basic dye, respectively. Three solutions containing five dyes are used in the polychromatic PAP stain. The same gynecologist performs colposcopy for patients with visual abnormal lesion or abnormal pap smear using the same, and a biopsy is taken from the suspicious area for histopathologic analysis.

**Steps of Colposcopic examination:** The steps involved in a colposcopic examination are as follows: first, wash your cervix with saline solution; next, check for any abnormal lesions and examine the vascularity; finally, apply 5% acetic acid solution and examine your cervix to look for any abnormal areas that appear to be white lesions and evaluate the vascularity, size, and degree of whiteness; finally, apply Lugol's iodine to look for abnormal areas that were iodine negative.

**Lugol's iodine solution:** Ten grams of potassium iodide (KI), five grams of iodine, and one hundred milliliters of distilled water. Dissolve the KI in twenty to thirty milliliters of distilled water. Add the iodine and heat slowly while stirring constantly until the iodine dissolves. Dilute to one hundred milliliters with distilled water and store in an amber glass stoppered bottle in the dark. A biopsy was performed for any abnormal lesions and was sent for

**Statistical Analysis:** SPSS version 23 was used for data processing, checking, entering, and analyzing the data. The present study's data were analyzed using the following statistical techniques. For qualitative components, the data were expressed as numbers and percentages, and for quantitative variables, as mean plus standard deviation (SD). Use chi-square test ( $\chi^2$ ) to find out if row and column variables are connected. The exact Fisher test: To determine if there are non-random correlations between two category variables.

### Results:

**Table (1,2)** declare insignificant difference in age across different PAPA finding (normal, inflammatory, abnormal). The p-value of 0.24 indicates that age is not strongly associated with smear outcomes. The distribution of parity across smear result groups shows no significant association (p-value 0.43).

**Table (3) & figures (1-4)** showed that the results of the Pap smear among the studied cases revealed that 43.3% of cases were normal, 38.3% showed inflammatory changes, and 18.3% were abnormal. Among the abnormal results, 3.3% were classified as Low Grade Squamous Intraepithelial Lesion (LG SIL), 11.7% were identified as Atypical Squamous Cells of Undetermined Significance (ASCUS), and 3.3% showed both ASCUS and atypical endocervical glands.

**Table (4) & figures (5-7)** showed most common findings in colposcopy.

**Table (5)** showed that there's no significant association between delivery method (Cesarean Section, Normal Vaginal Delivery, or both) and PAP smear outcomes (p-value 0.49).

**Table (6)** showed that there is a correlation between abnormal PAP smear and complaint of the patients attending outpatient clinic of obstetrics & gynecology with significant association between them (p-value 0.006).

### Discussion

Women with abnormal PAP smear results in this study had a median age of  $35.91 \pm 5.68$  years, which is marginally older than the median age of women with negative PAP smear results ( $34.73 \pm 4.84$  years). There was no discernible correlation between parity and the frequency of positive PAP smear results ( $p > 0.05$ ).

**Wang et al. (8)** discovered that the occurrence of cervical epithelial changes was associated with an older age group, which is consistent with the current study. This makes sense because women are more susceptible to the risk factors for cervical cancer as they age. (8)

The current investigation found that, although parity increased the incidence of positive PAP smear results (20% for parity  $< 3$  versus 17.6 for parity  $\leq 3$ ), which is statistically significant. **El-Moselhy et al. (9)** found that multiparity  $< 5$  is a major risk factor for cervical epithelial changes (31.4% in the CIN group and 14% in the non-CIN group), which is consistent with our results (P value = 0.361). Conversely, Chih et al. (10) discovered that there was no significant correlation between parity and the mean for the CIN group (1.9) and the non-CIN group (2.1).

A possible explanation of this association is the immune suppression during pregnancy, hormonal influences on cervical epithelium, and physical trauma related to vaginal deliveries. (9).

In present study, 26 women (43.3%) had negative results for abnormal PAP smear, while 11 women (18.3%) had positive results, 7 of them (11.7%) were ASCUS, 2 (3.3%) were LSIL, 2 (3.3%) case had atypical endocervical glands.

Nevertheless, **Sayed et al. (11)** discovered that using COCs had a protective impact on CIN.

Similar findings were published by **Jasem et al. (5)**, who discovered that 8.3% of women had not used COCs, and 26.5% of women who had used COCs had positive PAP smear results.

Additionally, users of COCs had a higher risk of cervical changes according to **Roura et al. (12)**.

**Oh et al. (13)** also noted that the usage of COCs was linked to a higher incidence of CIN II & III but had no influence on the risk of CIN I.

**El-Moselhy et al (9)** arrived to a similar conclusion, observing no statistically significant variation in the prevalence of COC use between women who had abnormal PAP screening results (96.1%) and those who had negative results (92%).

**Adhikari et al. (14)** also discovered that while oral contraceptives did not increase the occurrence of CIN, COCs may be protective against CIN after it has occurred.

Our study's conclusions indicate that using multiple oral contraceptives may cause increased unprotected

sexual activity, which increases the risk of HPV infection and other STDs and subsequent consequences for women, .

Among the patients in this investigation, leukoplakia and aberrant vasculature were the most often observed colposcopic findings. **Abd-El-Fatah et al. (16)** investigation revealed a similar conclusion.

In this study, of the cases with abnormal PAP, 6 had prior vaginal deliveries, 3 had only vaginal deliveries, and 2 had both vaginal & CS. In contrast, of the women with negative PAP smears, 14 had prior vaginal deliveries, 3 had only vaginal deliveries, and 9 had both vaginal & CS, with a non-significant (P value of 0.49).

Conversely, **El-Moselhy et al. (9)** said that an important risk factor for cervical neoplasia is vaginal birth. Of the 49 cases in the CIN group, 47 had a normal vaginal birth and 67 of the 92 cases in the normal group had a vaginal birth.

Conversely, **Chih et al., (10)** discovered a negative correlation between the onset of cervical neoplasia and long-term COC consumption.

Additionally, **Roura et al., (13)** discovered that the length of time using oral contraceptives was linked to a markedly higher risk of cervical cancer and CIN3/CIS (RR = 1.8 and 1.6, respectively, for those under 15 years old against those over 15 years old).

Also in support of our study, **Oh et al., (14)** found that the relative risk of CIN increased with the duration of COCs use (RRs of 1.1 and 2.2 for < 5 years and >10 years respectively).

Our results may be explained by the mitogenic effect of estrogen and progesterone on the cervical cells which undergo metaplastic changes under long term exposure to both hormones. **(14)**

Also **Xu et al., (15)** found that the risk of cervical neoplasia increases with increasing duration of hormonal contraceptive use .

Contact bleeding and abnormal discharge were the main complain of patients with abnormal PAP finding, compared with patient with normal PAP who presented less frequently with these symptoms. Number of cases presented by contact bleeding 10 while cases presented by vaginal discharge 49 however cases presented by both is 1.

#### **Conclusion:**

Abnormal cytology was reported in 18.3% of combined oral contraceptive pill users (11 out of 60 cases). Among these, the rates of ASCUS were 11.7%, Low Grade Squamous Intraepithelial Lesion (LSIL) 3.3%, and Atypical Glandular Cells (AGC) 3.3%. The length of time taking combination oral contraceptives was found to be positively correlated with dysplastic epithelial changes in Pap smear; longer term use of these contraceptives was associated with a greater grade of abnormal cytology.

**Conflict of interest:** the authors declare that they have no conflict of interest.

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