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ORIGINAL ARTICLE

Cervical Cytological and Colposcopic abnormalities in Cases Using Combined Oral Contraceptive Pills

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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 using combined oral contraceptive pills undergo examination in outpatient clinics of the hospital of Zagazig University. This examination includes a PAP smear with colposcopic visualization if there are abnormal findings in the PAP smear 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 Lesions (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). **Conclusions**: Abnormal cytology is related substantially to long-term oral contraceptive pill use.

Keywords: PAP smear, Cervical Colposcopic, Combined Oral Contraceptive Pills

INTRODUCTION

A significant amount of epidemiological evidence indicates that using oral contraceptives for an extended period may raise the risk of cervical cancer [1].

Cervical neoplasms are linked to persistent infection by oncogenic subtypes of the HPV (Human Papillomavirus) virus, particularly HPV-16 and HPV-18, which account for approximately 70% of cervical cancers. While HPV infection is a necessary factor, it is not sufficient for the development of uterine cervical cancer, as the virus is widely spread among women worldwide. In addition to factors related to HPV infection, factors related to immunity, genetics, and sexual behaviour can also influence the appearance of precursor lesions or cancer. Intrinsic factors include age, gender, ethnicity, race, genetic inheritance or

heredity. Extrinsic factors include smoking and alcoholism, inadequate eating habits, a sedentary lifestyle, obesity, and occupational exposure, among others [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 cervical cancer screening. 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].

To gather the samples, a cotton bud, a tiny brush, or an Ayer's spatula—a tiny wooden spatula—can be used. The presence of abnormal cells is an indicator of a positive test, which could indicate cancer directly or chronic irritation caused by a localized 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.

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 gynecology and obtained Institutional approval.

Inclusion criteria: Patients using combined oral contraceptive pills for more than one year an age range between 18 to 50 years.

Exclusion criteria: cases with cervical cancer or dysplasia in routine screening. Women use other hormonal contraceptive methods as injectable contraceptive compounds or on progestin-only pills. Women who have another 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 dyes, respectively. Three solutions containing five dyes are used in the polychromatic PAP stain. The same gynecologist performs colposcopy for patients with visual abnormal lesions 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 the chi-square test (X2) 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) declares insignificant differences in age across different PAPA findings (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 Lesions (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 the 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) shows that there is a correlation between abnormal PAP smears and complaints of the patients attending the outpatient clinic of obstetrics & gynecology with a significant association between them (p-value 0.006).

Table (1) Relation between Demographic data and PAP smear findings among the studied cases:

Variable		Smear						F	P
		Normal (*n*=26)		Inflammatory (n=23)		Abnormal (n=11)			
Age: (years)	*Mean ± Sd*	34.73±4.84		32.57±6.86		35.91±5.68		1.48	0.24
	Range	24-48		25-53		28-46			NS
Variable		**No**	**%**			**No**	**%**	χ^2	**P**
Parity:	*1-2*	7	41.2	7	41.2	3	17.6		
	3-4	15	39.5	16	42.1	7	18.4	3.81	0.43
	5-6	4	80	0	0	1	20		NS

SD: Standard deviation F: ANOVA test χ^2: Chi square test NS: Non-significant (P>0.05)

Table (2) Relation between PAP smear results and gynecological history among the studied cases:

Variable		Smear						F	P
		Normal (*n*=26)		Inflammatory (n=23)		Abnormal (n=11			
Age of 1st coitus:	*Mean ± Sd*	19.88±2.54		19.52±1.9		18.73±1.49		1.12	0.33
	Range	17-26		18-25		17-20			NS
Age of using COC:	*Mean ± Sd*	28.64±5.62		28.57±6.46		27.91±8.58		0.05	0.95
	Range	20-46		19-48		20-44			NS
Variable		**No**	**%**	**No**	**%**	**No**	**%**	χ^2	**P**
Duration of using COC:	*1-5 y*	12	44.4	14	52	1	3.6		
	5-10 y	11	47.7	8	34.7	4	17.6	16.61	0 .00229
	>10 y	3	30	1	10	60	50	5.	

SD: Standard deviation F: ANOVA test χ^2: Chi square test NS: Non-significant (P>0.05)

Table (3) Results of PAP smear among the studied cases:

Variable		(n=60)	
		No	%
Smear:	Normal	26	43.3
	Inflammatory	23	38.3
	Abnormal	11	18.3
Results:	Low Grade Squamous Intraepithelial Lesion (LG SIL)	2	3.3
	Atypical Squamous Cells of Undetermined Significance (ASCUS)	7	11.7
	Atypical endocervical gland	2	3.3

Table (4) Findings of colposcopy and pathology among the studied cases:

Variable		(n=60)	
		No	%
Colposcopy:	Not done	49	81.7
	Done	11	18.3
Findings:	Leukoplakia	4	6.7
	Abnormal Vasculature	3	5
	Ectopy	2	3.3
	Acetowhite area	2	3.3
Pathology results:	Normal	5	8.3
	Low Grade Squamous Intraepithelial Lesion (LG SIL)	4	6.7
	High Grade Squamous Intraepithelial Lesion (HG SIL)	2	3.3

Table (5) Relation between obstetric history & PAP smear findings among the studied cases:

Variable		Smear						χ^2	P
		Normal (*n*=26)		Inflammatory (n=23)		Abnormal (n=11)			
		No	%	No	%	No	%		
Previous delivery:	*CS*	14	45.2	11	35.5	6	19.4		
	NVD	3	23.1	7	53.8	3	23.1	3.44	0.49
	Both	9	56.3	5	31.3	2	12.5		NS

χ^2: Chi square test NS: Non-significant (P>0.05) *: Significant (P<0.05)

Table (6) Relation between complain & PAP smear findings among the studied cases:

Complain	Smear finding						χ^2	P
	Normal		Inflammatory		Abnormal			
	No	%	No	%	No	%		
Vaginal discharge	9	42.9	17	34.7	11	22.4	14.47	0.006*
Contact bleeding	0	0	2	20	8	80		
Both	0	0	0	0	1	100		

χ^2:Chi square test NS: Non-significant (P>0.05)

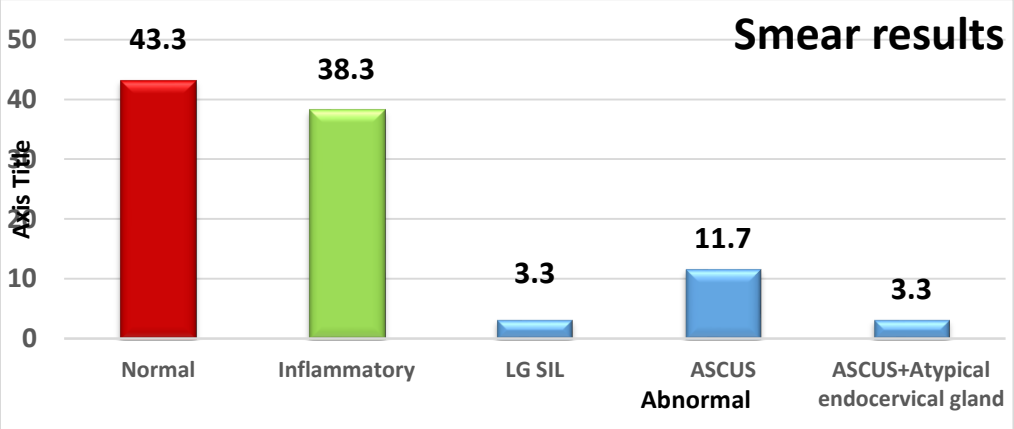

Figure 1: Results of PAP Smear among the studied cases.

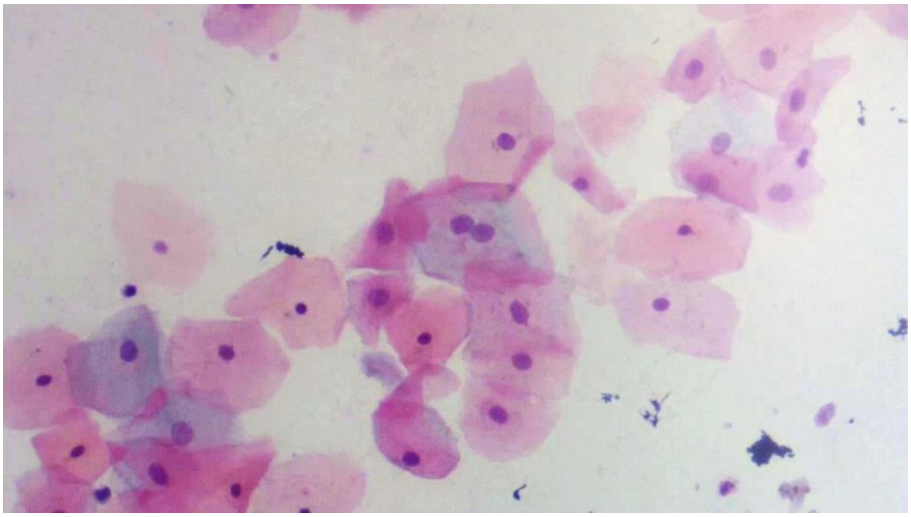

Figure 2: PAP smear showing normal squamous cells (PAPX200).

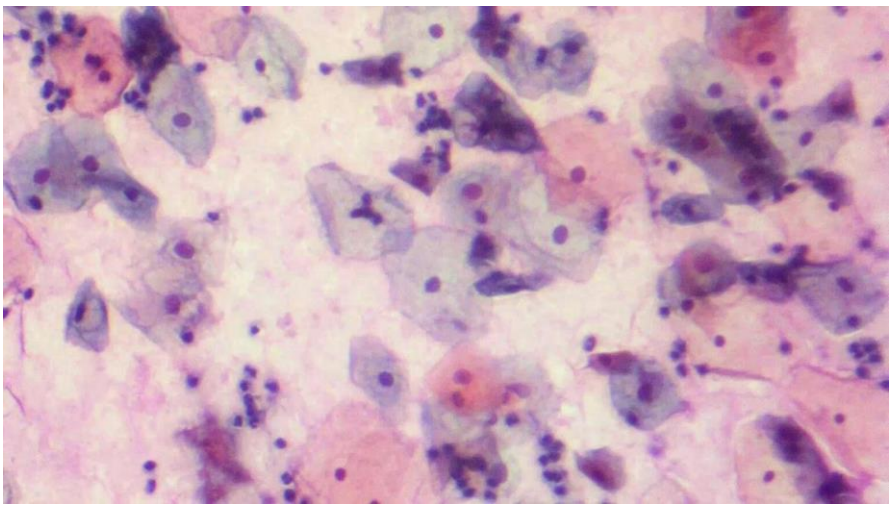

Figure 3: PAP smear from case of ASCUS showing cells with atypical mitosis, koilocytosis and some cells show enlarged nuclei and binucleation. (PAPX200).

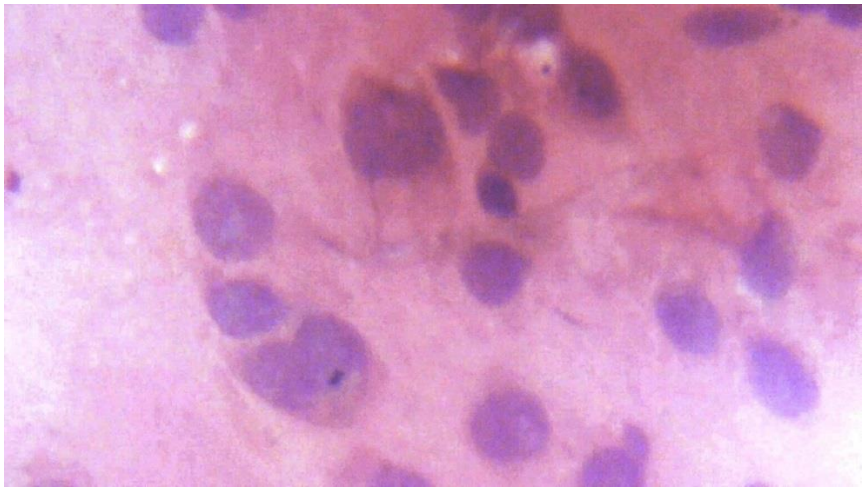

Figure 4: PAP smear of HSIL showing pleomorphic cells with large hyperchromatic nuclei (PAPX400).

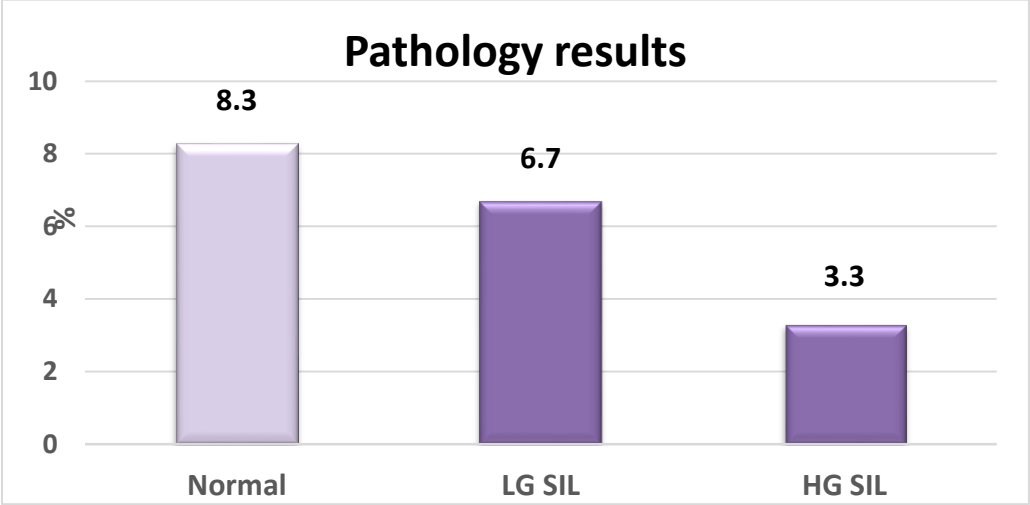

Figure (5): Pathology results among the studied cases had colposcopy.

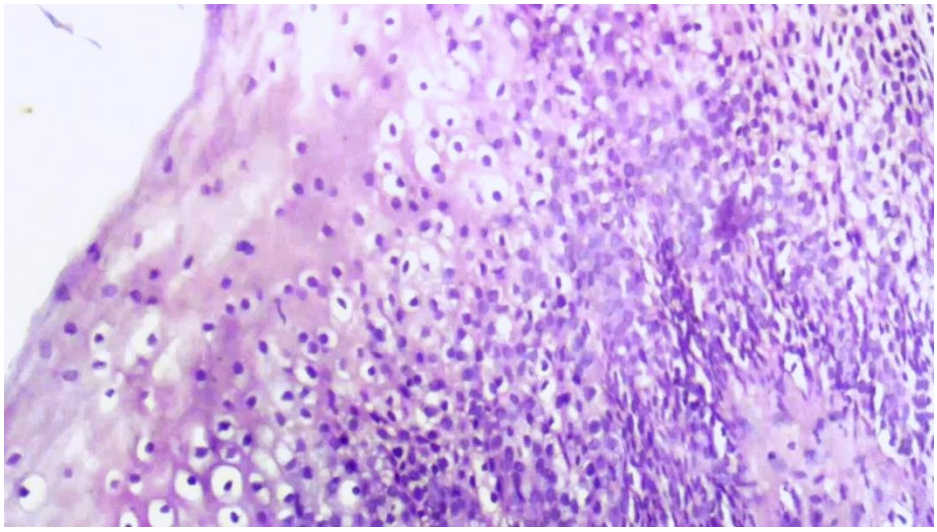

Figure 6: punch biopsy from cervix showing CINII (HSIL), dysplasia involving the lower 2/3of the squamous epithelium (H&E x200).

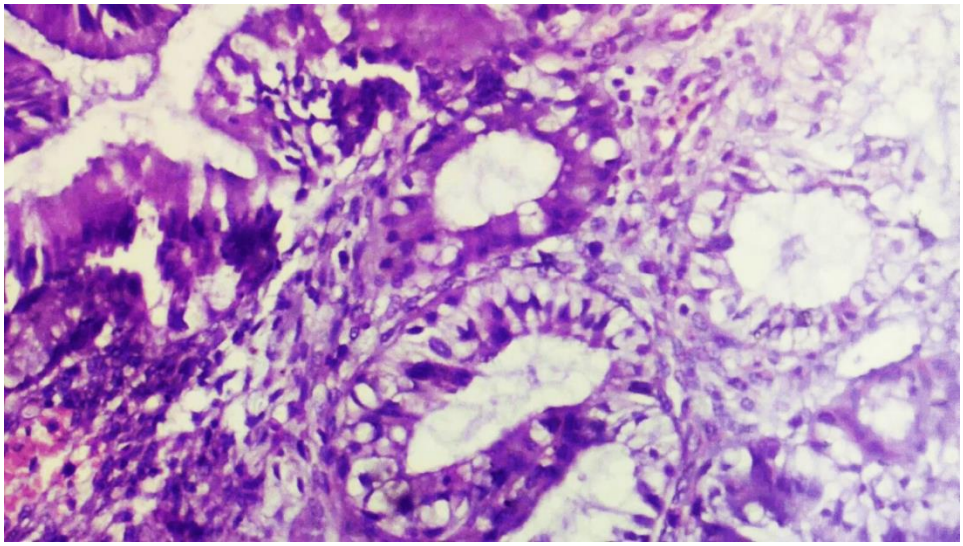

Figure 7: punch biopsy from cervix showing endocervical gland dysplasia (H&Ex200).

DISCUSSION

Women with abnormal PAP smear results in this study had a median age of 35.91±5.68 years, which is marginally older than the median age of women with negative PAP smear results (34.73±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 ≤ 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 the 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. [12], 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. [13]. Oh et al. [14] 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 at 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. [15] 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. Also Xu et al., [17] found that the risk of cervical neoplasia increases with increasing duration of hormonal contraceptive use. Contact bleeding and abnormal discharge were the main complaints of patients with abnormal PAP findings, compared with patients with normal PAP who presented less frequently with these symptoms. Several cases presented by contact bleeding was 10 while cases presented by vaginal discharge were 49 however cases presented by both is 1.

CONCLUSIONS

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.

Conflicts of Interest

The authors report no conflicts of interest.

FUNDING INFORMATION

None declared

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