

Evaluation of nonneoplastic findings on vaginal smears with comparison of intrauterine devices and oral contraceptive pill effects

Rahime BEDİR FINDİK^{1*}, Servet GÜREŞÇİ², Ayşe Nurcan ÜNLÜER³, Jale KARAKAYA⁴

¹Department of Obstetrics and Gynecology, Keçiören Education and Research Hospital, Ankara, Turkey

²Department of Pathology, Keçiören Education and Research Hospital, Keçiören, Ankara, Turkey

³Department of Obstetrics and Gynecology, Bilecik Central Hospital, Bilecik, Turkey

⁴Department of Biostatistics, Faculty of Medicine, Hacettepe University, Ankara, Turkey

Received: 24.03.2012 • Accepted: 19.07.2012 • Published Online: 15.03.2013 • Printed: 15.04.2013

Aim: Although the Pap smear is a common screening test for cervical cancer and its precursors, it can detect some benign conditions as well. In this study, the aim was to evaluate smear results with regard to nonneoplastic findings and to compare them to the detectable effects of intrauterine devices (IUDs) and oral contraceptive pills (OPs).

Materials and methods: In this retrospective study, the hospital records and cytopathology reports of 4248 patients were recorded. Smear results were evaluated according to the 2001 Bethesda System and were evaluated according to age groups, menopausal/menstrual status, physical examination findings, and contraceptive method usage.

Results: Of the 4248 patients, 75% were menstruating and 25% were menopausal. The most common smear result was nonspecific inflammation (NSI). In comparing the IUD (n = 730) and OP (n = 322) groups, we found *Candida* species, *Actinomyces*, and bacterial vaginosis to be significantly higher in the IUD-using group, while NSI, discharge, and erosion were found to be significantly higher in the OP group.

Conclusion: Pap smears can provide information about infectious diseases that can occur in the cervicovaginal region. These results reflect the fact that the IUDs disrupt vaginal flora more than OPs do.

Key words: Smear, oral contraceptive pill, intrauterine device, erosion, discharge

1. Introduction

The Pap smear is a screening test carried out by spreading cells taken from the inner and outer part of the uterine cervix on a glass slide. It was developed by George Papanicolaou in 1943 and is named after him. It is a simple, rapid, and painless procedure performed during speculum examination by clinicians. Cells are obtained, placed on a glass slide, rinsed with liquid fixative, and sent to a pathology laboratory for examination (1–5).

Although the Pap smear is a common screening test for cervical cancer and its precursors, it can detect some benign conditions, as well (1,6). In the present study, 4248 smear results were reviewed in order to determine their relation with age, menopausal status, contraceptive history, and physical examination findings.

2. Materials and methods

In this retrospective study, the hospital records and cytopathology reports of 4248 women who were referred

to the Department of Gynecology and Obstetrics at Keçiören Education and Research Hospital between September 2006 and September 2009 were examined. Smears were taken from the internal and outer surfaces of the cervix using a brush and were spread on a glass slide. They were fixated with alcohol to protect cells from harm and were sent to a pathology laboratory. Slides were stained using the Papanicolaou (Pap) technique and were evaluated according to the 2001 Bethesda standards as formerly described (7). Results were classified as normal smear (NS), nonspecific inflammation (NSI), *Candida* species (CS), shift of flora suggestive of bacterial vaginosis (BV), *Trichomonas vaginalis* (TV), *Actinomyces* species (AS), atrophic vaginitis (AV), and atypia of undetermined significance (ASC-US).

The patient's age, menstruation or menopausal status, physical examination findings (erosion and discharge), and contraception method used, if any, were all recorded. Contraceptive methods noted were intrauterine

* Correspondence: drbedir75@yahoo.com

contraceptive devices (IUDs) and oral contraceptive pills (OPs). Patients were divided into 4 age groups for statistical analysis: 0–20 years, 21–40 years, 41–50 years, and over 51 years.

Results were expressed by frequency analysis. The significance of intergroup differences was studied with SPSS 16.0 (SPSS Inc., Chicago, IL, USA) by chi-square test. $P < 0.05$ was considered statistically significant.

3. Results

Of the 4248 patients, 3188 (75%) were menstruating and 1060 (25%) were menopausal. Smear results were found as follows: 12% were NS ($n = 511$), 65.1% were NSI ($n = 2766$), 5.1% were CS ($n = 218$), 5.6% were BV ($n = 237$), 1.4% were TV ($n = 57$), 0.09% were AS ($n = 38$), 9% were AV ($n = 383$), and 0.8% were ASC-US ($n = 24$).

Smear results according to age groups are shown in Table 1. The corresponding results in menopausal and menstruating patients are shown in Table 2.

As a result of contraceptive method analysis, it was found that 17.2% of the patients used an IUD and 7.8% used OPs. The rates of NSI were 71% and 81% among those who used IUDs and OPs, respectively. The difference between the IUD and OP groups was found to be statistically significant. The rates of AS were 4% and 0% in those who used IUDs and OPs, respectively, with a statistically significant difference. The rate of BV was 7% and 2.7% in the IUD and OP groups, respectively, with a statistically significant difference. The rate of CS was 7.3% in those using IUDs, while it was 3.9% in those who used OPs. The difference was statistically significant. The rate of NS was 7% in the IUD group, while it was 9.6% in the OP group, with a statistically significant difference between groups. The rates of AV, TV, and ASC-US were not statistically significant between the 2 groups. Discharge was present in 56% of the patients using IUDs and 68.9% of those using

OPs, with a significant difference between them. Erosion was found in 6.7% of those using IUDs and 7.5% of those using OPs, with a statistically significant difference (Table 3).

4. Discussion

The Pap smear is a screening test that can be carried out readily during gynecological examination. It should be conducted once a year in women of reproductive age (1). Although the Pap smear was developed for cervical cancer screening, it is obvious that it sheds light on nonneoplastic pathologies, as well (1,6).

In this community-based study carried out with quite a large sample, it can be observed that ASC-US occurred at low rates in smear results, and nonneoplastic findings were detected far more commonly. ASC-US reflects a pathological diagnosis rather than a clinical diagnosis and patient follow-up is necessary. Our ASC-US rates (0.8%) were lower than those rates in the previous literature from Turkey, which reported an overall rate of 1.07%, but in reality our rates were similar to some of the individual participant hospitals' rates (0.6%, 0.7%) from that study (8).

In the evaluation of all smear results, it was seen that NSI was the leading result, followed by NS and AV, which were expected to be high in menopausal women. Following them, BV, CS, TV, AS, and ASC-US were found in decreasing order of frequency. The high rate of NSI is compatible with the results of previous studies. This shows that there is cervical inflammation in the majority of women in the community, even if it is not specific (1).

In the evaluation of age groups, NSI is most common in the age group of 20–40 years, followed by 41–50 years, 0–20 years, and over 50 years. It can be concluded from these results that NSI occurs mostly in women of child-bearing age. NSI occurs less frequently in women over 50, suggesting that in sexually active women of reproductive

Table 1. The distribution of nonneoplastic smear results according to age (frequency analysis; percentage (number)).

Characteristics	N	NSI	BV	CS	AS	TV	AV	ASC-US
Age 0–20 2.3% (99)	24.2% (24)	65.7% (65)	3% (3)	5.1% (5)	0% (0)	1% (1)	0% (0)	1% (1)
Age 21–40 49.1% (2084)	10.8% (226)	72.7% (1515)	6.2% (130)	7% (146)	1% (20)	1.1% (22)	0.3% (7)	0.8% (17)
Age 41–50 28.8% (1223)	12.9% (158)	68.3% (835)	5.6% (69)	3.8% (47)	1.3% (16)	2.1% (26)	5.2% (63)	0.7% (9)
Age > 50 19.8% (842)	12.2% (103)	41.6% (350)	4.2% (35)	2.4% (20)	0.2% (2)	1.3% (11)	37% (313)	1% (8)

Table 2. The distribution of nonneoplastic smear results according to menopausal status (frequency analysis; percentage (number)).

Characteristics	N	NSI	BV	CS	AS	TV	AV	ASC-US
Menstrual 75% (3188)	11.6% (371)	72% (2297)	5.9% (188)	5.8% (185)	1.1% (36)	1.5% (48)	1.2% (39)	0.8% (24)
Menopausal 25% (1060)	13.2% (140)	44% (469)	4.6% (49)	3.1% (33)	0.2% (2)	1.1% (12)	32.5% (344)	1% (11)

Table 3. Comparison of intrauterine device (IUD) and oral contraceptive pill (OP) findings (chi-square test; percentage (number)).

Characteristic	IUD 17.2% (730)	OP 7.8% (322)	P-value
NSI	71.6% (522)	81% (269)	0.0018
BV	7% (51)	2.7% (9)	<0.001
CS	7.3% (53)	3.9% (13)	<0.001
AS	4% (29)	0% (0)	<0.001
TV	1.8% (13)	1.5% (5)	0.2287
AV	0.5% (4)	0.6% (2)	0.5008
ASC-US	0.8% (6)	0.6% (2)	0.2480
Erosion	6.7% (49)	7.5% (25)	0.0088
Discharge	56% (408)	63.9% (212)	0.0144

age, the flora of the vagina is more susceptible to inflammation. This shows the effects of sexual life on smear results.

In comparing the smear results of women of reproductive age with those who are in menopause, it can be seen that NSI was predominant in both groups, although it was more common in women of reproductive age. Following in frequency were the NS results. In the menopausal group, AV was markedly high. This result is natural, given the effect of decreasing estrogen on cervicovaginal tissue during menopause. In the menopausal group, the vaginal microflora lacks lactobacilli due to the deficiency of estrogen, which sets the stage for atrophic vaginitis (9). Since almost half of the women over age 40 showed AV, local estrogen therapy, unless contraindicated, can be suggested for this group to aid sexual activity. In addition, in the menopausal group, ASC-US was found at a higher rate than in the menstruating group (1% and 0.8%, respectively). This result may be related to cytohormonal changes in menopause. In both groups, the most common cervical infections are BV and CS. Compared to other infectious agents, BV and CS are also the most common

agents in all age groups. If we evaluate results according to age groups, CS is predominant in both the age groups of 0–20 and 20–40 years, whereas in the 40–50 group, BV becomes more common. In the age group of those over 50, the rates of BV and CS fall as low as 4.2%. CS is most common in the younger age group. In the other reproductive age groups, BV and CS rates are comparable, and both rates decrease with age. In view of these results, along with previous ones, it can be stated that smears are valuable in the diagnosis of infectious pathologies such as BV and CS (6).

In our study, the TV prevalence rate was found to be 1.4%, which was consistent with a previous study from Iran, which reported a rate of 0.9%. *Trichomonas vaginalis* is referred to as a sexually transmitted disease, and this similarity in prevalence may be due to the comparable developmental status and religion of the 2 countries, where religious life inhibits the taking of multiple partners (10). However, an epidemiologic study from Palestine reported a prevalence rate of 18.2%, which is very high compared to the above-mentioned studies (11). This reflects the effect of developmental status on infectious diseases in countries.

In the present study, smear results were compared between 730 subjects who used an IUD and 322 who used OPs. Results showed significantly higher degrees of NSI in the OP group. Increased inflammation may be due to the decrease in lactobacilli caused by the cytohormonal effects of OP use on cervicovaginal flora (12).

The rate of BV was found to be significantly higher in the IUD group than in the OP group, which is compatible with the results of previous studies, which support the relationship between IUDs and BV (13). *Gardnerella vaginalis* is an anaerobic microorganism found in normal flora. IUDs exert long-term contraceptive effects by spreading copper in uterine secretions (14) and through negative effects on lactobacilli. They may cause an increase in anaerobic microorganisms such as *Gardnerella vaginalis*, and hence the increase of BV (15,16).

Similarly, in the IUD group, the rate of CS was significantly higher than in the OP group. In some previous studies, the effect of OP use on vaginal flora was emphasized, but it was not compared with the effect of IUD use on vaginal flora. In our comparative study, the relationship between BV, CS, and IUD use is very clear (12), suggesting that the IUD may impair vaginal flora more than OP use does (17) (Figures 1 and 2).

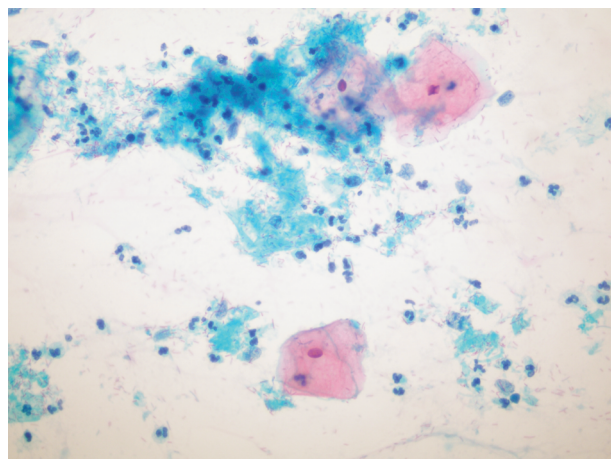


Figure 1. Nonspecific inflammation in an OP user. Note lactobacilli in background (conventional preparation, Pap 400×).

As shown in previous studies, there was a remarkable rise in AS in the IUD group (17,18). AS colonization is mostly seen in cases of long-term IUD usage (18). The fact that AS was not diagnosed in non-IUD users in our study is also compatible with this theory. In the absence of symptoms, IUD removal or antibiotherapy is not recommended, but if AS is determined through a Pap smear, the patient should be reexamined for symptoms (19,20).

In addition, when comparing the 2 groups with regard to discharge and erosion, both symptoms were found at significantly higher rates in the OP group. According to our results, despite studies supporting the protective effect of OP on vaginal flora (21), both OPs and IUDs produce effects impairing vaginal flora, with the effect of IUDs appearing to be stronger (17). There was no significant difference between the IUD and OP groups in terms of AV, TV, and ASC-US.

In conclusion, Pap smears can provide useful information about infectious diseases that can occur in the cervicovaginal region. These results reflect the fact that IUDs disrupt vaginal flora more than OPs do. Studies on this issue are limited, and population-based studies confirmed with microbiologic tests are required.

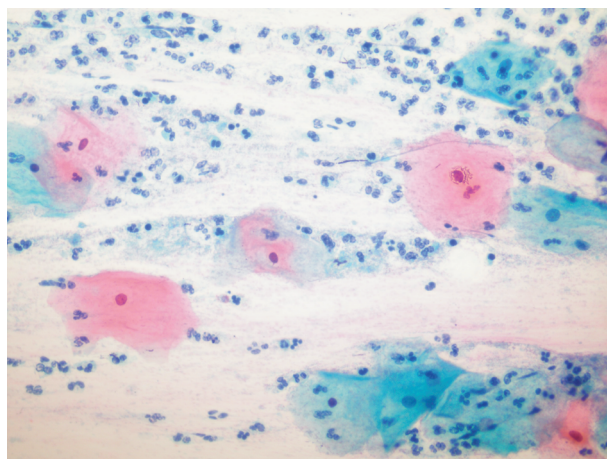


Figure 2. Shift in flora suggestive of bacterial vaginosis in an IUD user. Note coccobacilli in the background (conventional preparation, Pap 400×).

References

1. Bukhari MH, Majeed M, Qamar S, Niazi S, Syed SZ, Yusuf AW et al. Clinicopathological study of Papanicolaou (Pap) smears for diagnosing of cervical infections. *Diagn Cytopathol* 2012; 40: 35–41.
2. Powers CN. Diagnosis of infectious diseases: a cytopathologist's perspective. *Clin Microbiol Rev* 1998; 11: 341–65.
3. Michalas SP. The Pap test: George N. Papanicolaou (1883–1962). A screening test for the prevention of cancer of uterine cervix. *Eur J Obstet Gynecol Reprod Biol* 2000; 90: 135–8.
4. Papanicolaou GN. A new procedure for staining vaginal smears. *Science* 1942; 95: 438–9.

5. Vuopala S, Klemi PJ, Mäenpää J, Salmi T, Mäkäräinen L. Endobrush sampling for endometrial cancer. *Acta Obstet Gynecol Scand* 1989; 68: 345–50.
6. Eriksson K, Forsum U, Bjornerem A, Platz-Christensen JJ, Larsson PG. Validation of the use of Pap-stained vaginal smears for diagnosis of bacterial vaginosis. *APMIS* 2007; 115: 809–13.
7. Nayar R, Solomon D. Support from authors of the Bethesda system. *Cytopathology* 2008; 19: 399–400.
8. Turkish Cervical Cancer and Cervical Cytology Research Group. Prevalence of cervical cytological abnormalities in Turkey. *Int J Gynaecol Obstet* 2009; 106: 206–9.
9. Gupta S, Kumar N, Singhal N, Manektala U, Jain S, Sodhani P. Cytohormonal and morphological alterations in cervicovaginal smears of postmenopausal women on hormone replacement therapy. *Diagn Cytopathol* 2006; 34: 676–81.
10. Chalechale A, Karimi I. The prevalence of *Trichomonas vaginalis* among patients that presented to hospitals in the Kermanshah district of Iran in 2006-2007. *Turk J Med Sci* 2010; 40: 971–5.
11. Al-Hindi AI, Lubbad AMH. *Trichomonas vaginalis* infection among Palestinian women: prevalence and trends during 2000-2006. *Turk J Med Sci* 2006; 36: 371–5.
12. Cherpes TL, Marrazzo JM, Cosentino LA, Meyn LA, Murray PJ, Hillier SL. Hormonal contraceptive use modulates the local inflammatory response to bacterial vaginosis. *Sex Transm Infect* 2008; 84: 57–61.
13. Demirezen S, Küçük A, Beksaç MS. The association between copper containing IUCD and bacterial vaginosis. *Cent Eur J Public Health* 2006; 14: 138–40.
14. Zipper JA, Tatum HJ, Pastene L, Medel M, Rivera M. Metallic copper as an intrauterine contraceptive adjunct to the “T” device. *Am J Obstet Gynecol* 1969; 105: 1274–8.
15. Smayevsky J, Canigia LE, Lanza A, Bianchini H. Vaginal microflora associated with bacterial vaginosis in nonpregnant women: reliability of sialidase detection. *Infect Dis Obstet Gynecol* 2001; 9: 17–22.
16. Demirezen S. Review of cytologic criteria of bacterial vaginosis: examination of 2,841 Papanicolaou-stained vaginal smears. *Diagn Cytopathol* 2003; 29: 156–9.
17. Ocak S, Cetin M, Hakverdi S, Dolapcioglu K, Gungoren A, Hakverdi AU. Effects of intrauterine device and oral contraceptive on vaginal flora and epithelium. *Saudi Med J* 2007; 28: 727–31.
18. Tendolkar U, Pandit D, Khatri M, Deodhar L. *Actinomyces* species associated with intrauterine contraceptive devices and pelvic inflammatory disease. *Indian J Pathol Microbiol* 1993; 36: 238–44.
19. Mao K, Guillebaud J. Influence of removal of intrauterine contraceptive devices on colonisation of the cervix by actinomyces-like organisms. *Contraception* 1984; 30: 535–44.
20. Westhoff C. IUDs and colonisation or infection with *Actinomyces*. *Contraception* 2007; 75: 48–5.
21. Batashki I, Markova D, Milchev N, Uchikova E, Gürova A. Effect of oral contraceptives on vaginal flora. *Akush Ginekolog* 2006; 45: 49–51.