**Cukurova Medical Journal**
ÇUKUROVA ÜNİVERSİTESİ TIP FAKÜLTESİ

Cukurova Med J 2021;46(1):81-87
DOI: 10.17826/cumj.784507

**ARAŞTIRMA / RESEARCH**

# Evaluation of gynecological complaints of women having inflammatory changes in their cervicovaginal smears

## Servikovajinal smearlarında inflamatuar değişiklikler bulunan kadınların jinekolojik şikayetlerinin değerlendirilmesi

Hanife Güler Dönmez[1], Mehmet Sinan Beksac[2]

[1]Hacettepe University, Faculty of Science, Department of Biology, Ankara, Turkey
[2]Hacettepe University Faculty of Medicine, Division of Perinatology, Department of Obstetrics and Gynecology, Ankara, Turkey

*Cukurova Medical Journal 2021;46(1):81-87*

**Abstract**

**Purpose:** Inflammatory Pap-test is reported commonly, however, there is no consensus on its clinical significance. This study was to investigate the presence of gynecological complaints such as vaginal discharge, pruritus, burning, odor, and pelvic/abdominal pain in women who are having inflammatory changes in their cervicovaginal smears.

**Materials and Methods:** The cervicovaginal smears of 854 women, between the ages of 18 and 76 (38.7 ± 11.18) years, were evaluated. Papanicolaou staining was used for cytological evaluation. For the diagnosis of inflammation, polymorphonuclear leucocytes (PMNLs) were counted in at least five visual fields (×100). PMNLs counts "above 40" were recorded as inflammation positive.

**Results:** Inflammation was detected in 115 of the 854 (13.5%) patients; these were considered the study group. Cytological specimens with various types of infections and epithelial cell abnormalities were excluded from the cohort (*n* = 221, 25.8%). Patients without any infection (*n* = 518, 60.7%) were accepted as the control group. In the study group, gynecological complaints including vaginal discharge, pruritus, burning, odor, and abdominal pain were found at rates of 56.5%, 6.1%, 3.5%, 4.3%, and 7.8%, respectively. The presence of vaginal discharge was statistically significant in women with inflammation (56.5%) compared to the control group (25.9%).

**Conclusion:** Vaginal discharge is significantly more frequent in women with inflammatory changes in their cervicovaginal smears.

**Keywords:**. Inflammation, Papanicolaou staining, vaginal discharge, cervicovaginal smears

**Öz**

**Amaç:** İnflamasyon Pap-testinde yaygın olarak rapor edilmektedir, ancak klinik önemi konusunda bir fikir birliği yoktur. Servikovajinal simirlerde inflamatuar değişiklikler olan kadınlarda vajinal akıntı, kaşıntı, yanma, koku, pelvik/karın ağrısı gibi jinekolojik şikayetlerin varlığını araştırılması amaçlanmıştır.

**Gereç ve Yöntem:** 18-76 (38.7 ± 11.18) yaşları arasındaki 854 kadının servikovajinal simirleri değerlendirildi. Papanicolaou boyama yöntemi sitolojik değerlendirme için kullanıldı. İnflamsyon teşhisi için, polimorfonükleer lökositler (PMNL'ler) en az beş görsel alanda (×100) sayıldı. "40'ın üzerindeki" PMNL sayıları, inflamasyon pozitif olarak kaydedildi.

**Bulgular:** 854 hastanın 115'inde (%13.5) inflamasyon tespit edildi; bunlar çalışma grubu olarak kabul edildi. Çeşitli enfeksiyon türleri ve epitel hücre anormallikleri olan sitolojik örnekler kohorttan çıkarıldı (*n* = 221, %25,8). Herhangi bir enfeksiyonu olmayan hastalar ise (*n* = 518, %60,7) kontrol grubu olarak kabul edildi. Çalışma grubunda vajinal akıntı, kaşıntı, yanma, koku ve karın ağrısı gibi jinekolojik şikayetler sırasıyla %56,5, %6,1, %3,5, %4,3 ve %7,8 oranında bulundu. İnflamasyonlu kadınlarda vajinal akıntı varlığı (%56.5) kontrol grubuna (%25.9) göre istatistiksel olarak anlamlıydı.

**Sonuç:** Vajinal akıntı, servikovajinal smearlarında inflamatuvar değişiklikler olan kadınlarda anlamlı olarak daha sıktır.

**Anahtar kelimeler**: İnflamasyon, Papanicolaou boyama yöntemi, vajinal akıntı, servikovajinal smear

Yazışma Adresi/Address for Correspondence: Dr. Hanife Guler Dönmez, Hacettepe University, Department of Biology, Faculty of Science, Ankara, Turkey E-mail: hnftnr@gmail.com
Geliş tarihi/Received: 24.08.2020 Kabul tarihi/Accepted: 21.09.2020 Çevrimiçi yayın/Published online: 10.01.2021

## INTRODUCTION

Inflammatory changes are reported frequently in Pap-stained cervicovaginal smears. However, their clinical significance is unclear. Moreover, there is no consensus on how to manage patients with inflammatory changes in their cervicovaginal smears[1]. Cervicovaginal inflammation might be related to a poor obstetric outcome and it may increase a patient's susceptibility to Human Papillomavirus and Human Immunodeficiency Virus (HIV) infections[2]. Furthermore, chronic inflammation may participate in the carcinogenesis process by enhancing the epithelial cell turnover[3].

Studies have also focused on investigating the relationship between inflammatory changes and genital infections[4,5]. Gynecological infections such as Bacterial vaginosis (BV), Chlamydiasis and Trichomoniasis (Tv) have been reported to be associated with inflammatory changes at cervicovaginal smears; however, according to Bertolingo, et al., 71% of patients with inflammation had no evidence of any specific microorganisms[6].

Gynecological complaints are the most frequent reasons for attending outpatient clinics to undergo gynecological examinations[7]. The most common complaints are vaginal discharge and abdominal pain[8]. Vaginal discharge is often related to genital infections such as BV, Tv, and Candidiasis depending on the vaginal pH changes[9]. Undergoing treatment based on the appearance of the discharge alone is not adequate and it frequently results in inappropriate treatment[10]. Abdominal pain can occur because of various reasons. Moreover, distinguishing it from pain related to the gastrointestinal system is very hard as they share the same visceral innervation. The most common factors associated with abdominal pain are pelvic inflammatory disease, ovarian cysts, endometriosis, and fibroids[8,11].

This study aimed to assess the association between gynecological complaints (such as vaginal discharge, pruritus, burning, odor, and abdominal pain) and the presence of inflammatory changes in the cervicovaginal smears of patients without any specific infection. We believe that this study will contribute to dissociate/differentiate "genital system infection" and "cytological inflammatory changes" concepts in the minds of physicians in routine practice.

## MATERIALS AND METHODS

This study was approved by the Hacettepe University Ethics Committee (reference number GO18/915-34) and it was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all individual participants included in this study.

### Sample

This study was conducted at the Department of Obstetrics and Gynecology, Hacettepe University between September 2018 and April 2020. Study population consisted of patients who attended the hospital for varied gynecological complaints or routine control. Smears were taken by an experienced gynecologist (MSB) and evaluated by an experienced cytologist (HGD). Before the pelvic examination, data on age, pregnancy outcomes, contraception methods, gravidity, and clinical symptoms were enrolled. The presence and color of vaginal discharge were recorded as the observation of gynecologist. Pruritus, burning, odor, and abdominal pain were enrolled as answers of patients. All of the required demographic and clinical data were obtained from the files of the patients and the electronic database of our institution (Table 1).

### Procedure

#### Papanicolaou staining

The cervicovaginal samples were taken using a sterile cytobrush and smearing on a slide. The slides were immediately fixed with ethanol (96%) without air dry. The fixed slides were immersed in the decreasing level of alcohol (85% to 50%) to distilled water. Rehydrated slides were stained with Harris' Hematoxylin (Merck, Germany) for 2 min. and rinsed under running tap water. Hydrochloric acid-alcohol (%1, v/v) was used for decoloring.

After washing the slides with distilled water and increasing alcohol series (50% to 85%), Orange G and EA 65 dyes (Merck, Germany) were performed, respectively. To clean off the excess dye, slides were washed with 95% ethanol after each staining step. The stained smears were immersed in Xylene 15 min., then Entellan (Merck, Germany) was used as a mounting medium. The cytological findings were investigated and photographed using a camera attached-light microscope (Leica DM 4000B).

### Cytological evaluation

In the cytological examination, fungal infection was diagnosed by detecting yeast and filamentous forms of fungi[12]. The diagnosis of BV was established by detecting clue cells as well as the absence of Lactobacilli, the lack of neutrophil leukocytes, and increase in the number of free cocci[13]. The diagnosis of trichomoniasis depend on the microscopic observation of motile protozoa[14].

For the detection of actinomycosis, dense basophilic central aggregations surrounded by intertwined filament-type formations[15]. Epithelial abnormalities were diagnosed depend on Bethesda system[16]. Then, specific infections including BV, fungal infection, Actinomycosis, Tv, and epithelial cell abnormalities were excluded from the cohort due to their possible effects on the gynecological complaints. Therefore, this cohort evaluated patients with inflammation (study group) and without any specific infection/epithelial abnormalities (control group).

To diagnosis inflammation, PMNLs were counted in at least five visual fields (×100). PMNLs counts "greater than 40" were recorded as inflammation[17]. Furthermore, macrophages, lymphocytes, enlarged nuclei, perinuclear halos, binucleation as well as nuclear degenerations including karyopyknosis, karyorrhexis, and karyolysis were also detected in inflammatory Pap-smears.

### Statistical analysis

Statistical Package for the Social Sciences (SPSS, version 23, IBM) were used for statistical analysis. Study and control groups were compared using the "Pearson Chi-square test", "Fischer's exact test" or Yates's Chi-square" depending on the expected count. A *P*-values < 0.05 were considered as statistically significant.

## RESULTS

Cervicovaginal smears ($n$ = 854) were obtained from between the ages of 18 and 76 years (38.73 ± 11.18). Inflammation was detected in 115 of 854 (13.5%) patients; these patients accepted as the study group. In turn, patients without any infection ($n$ = 518, 60.7%) were considered the control group. Cytological specimens with various types of infections and epithelial cell abnormalities were excluded from the cohort ($n$ = 221, 25.8%). Table 1 shows the clinical and demographic characteristics of the patients.

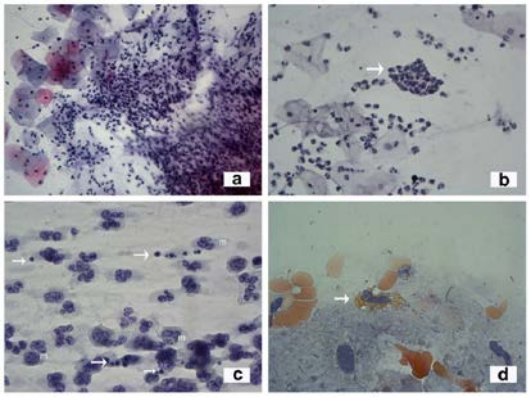


**Figure 1. Inflammatory Pap-smear. a) group of neutrophils covered almost all part of background, b) epithelial cell is totally covered by neutrophils (arrow), c) Apoptotic neutrophils (arrow) and macrophages (m) are seen around heathy neutrophils, d) degranulated eosinophil leucocyte (arrow) is depicted.**

Increased amounts of PMNLs (neutrophils and eosinophils) were demonstrated in the cervicovaginal smears of cases with inflammation (Figure 1a-d). Interestingly, the entire surfaces of some epithelial cells covered by neutrophils (Figure 1b). Moreover, apoptotic neutrophils were frequently observed in the inflammatory background (Figure 1c). In the study group, increased amounts of macrophages and lymphocytes were also found as well as PMNLs.

Cellular changes including enlarged nuclei, perinuclear halos, binucleation, and nuclear degenerations (karyopyknosis, karyorrhexis, and karyolysis) were also detected in inflammatory Pap-smears.

In the study group, gynecological complaints including vaginal discharge, pruritus, burning, odor, and abdominal pain rates were found to be 56.5%, 6.1%, 3.5%, 4.3%, and 7.8% respectively. Only, the presence of vaginal discharge was statistically significant in women with inflammation (56.5%) compared to control group (25.9%) ($P$ < 0.001). There was no statistically significant relationship between the other gynecological complaints and the presence of inflammation ($P$ > 0.05) (Table 2).

**Table 1. Clinical and demographic characteristics of the patients with and without inflammation**

| | Inflammation (+) (*n* = 115) | Inflammation (–) (*n* = 518) | Total (*n* =633) |
|---|---|---|---|
| Age (Mean ± SD) | 41.57 ± 12.20 | 38.66 ± 11.27 | 39.19 ± 11.491 |
| Gravida (Mean ± SD) | 2.41 ± 1.91 | 2.50 ± 2.05 | 2.48 ± 2.03 |
| Parity (Mean ± SD) | 1.48 ± 1.91 | 1.22 ± 1.17 | 1.27 ± 1.18 |
| Abortus (Mean ± SD) | 0.95 ± 1.53 | 1.28 ± 1.868 | 1.22 ± 1.815 |

SD: Std. Deviation

**Table 2. The relationship between gynecological complaints and the presence of inflammation**

| | Inflammation (+) | Inflammation (–) | Total | *P* |
|---|---|---|---|---|
| Vaginal discharge | | | | |
| *(–)* | 50 (43.5) | 384 (74.1) | 434 (68.6) | <0.001*,a |
| *(+)* | 65 (56.5) | 134 (25.9) | 199 (31.4) | |
| Pruritus | | | | |
| *(–)* | 108 (93.9) | 506 (97.7) | 614 (97.0) | 0.061b |
| *(+)* | 7 (6.1) | 12 (2.3) | 19 (3.0) | |
| Burning | | | | |
| *(–)* | 111 (96.5) | 507 (97.9) | 618 (97.6) | 0.493b |
| *(+)* | 4 (3.5) | 11 (2.1) | 15 (2.4) | |
| Odor | | | | |
| *(–)* | 110 (95.7) | 507 (97.9) | 617 (97.5) | 0.186b |
| *(+)* | 5 (4.3) | 11 (2.1) | 16 (2.5) | |
| Abdominal pain | | | | |
| *(–)* | 106 (92.2) | 486 (93.8) | 592 (93.5) | 0.660c |
| *(+)* | 9 (7.8) | 32 (6.2) | 41 (6.5) | |
| Total | 115 (100) | 518 (100) | 633 (100) | |

*:*P* < 0.001, a: Pearson Chi Square, b: Fisher's exact test, c: Yates's Continuitiy Correction test

Vaginal discharge was categorized according to color, labeling it as transparent, white, grey, brown, yellow, and yellowish-green. In the study group, vaginal discharge with grey and yellowish-green colors were most frequently seen colors with rates of 24.3% and 12.2%, respectively (Table 3).

**Table 3. Evaluation of vaginal discharge color**

| Vaginal discharge color | Inflammation (+) (*n* = 65) | Inflammation (–) (*n* = 134) | Total (*n* = 199) |
|---|---|---|---|
| White | 6 (5.2) | 47 (9.1) | 53 (8.4) |
| Grey | 28 (24.3) | 27 (5.2) | 55 (8.7) |
| Brown | 3 (2.6) | 8 (1.5) | 11 (1.7) |
| Yellow | 2 (1.7) | 4 (0.8) | 6 (0.9) |
| Yellowish-green | 14 (12.2) | 17 (3.3) | 31 (4.9) |
| Transparent | 12 (10.4) | 31 (6.0) | 43 (6.8) |

## DISCUSSION

Inflammation is commonly demonstrated at the Pap-stained cervicovaginal smears in clinical practice. However, the biological events behind inflammatory changes are still unclear and need to be investigated. In our previous study, inflammation was found in 11.6% ($n$ = 26/224) of our study group[18]; however, the prevalence of inflammation differs between one population and the other one (7.6% to 80.5%)[6,19,20]. In this study, the inflammation rate was 13.5%, which is consisted with previous studies.

Inflammation is a defense mechanism regulated by the inflammatory cells and the release of mediators including cytokines and chemokines[3]. After removal stimuli, undissolved inflammation becomes persistent. Chronic inflammation may participate in the carcinogenesis process relating to HPV infection by enhancing the epithelial cell turnover[3]. Furthermore, chronic inflammation may influence the squamous epithelium and it may increase the vulnerability of sexually transmitted diseases[2]. Inflammation affects cellular junctions including desmosomes, *zonula adherence,* and *zonula occludens*[21,22]. During the inflammation processes, local influx of cytokines causes the disassembly of junctional proteins[22-24]. Defects in the junctional proteins are not only important for the barrier function of epithelium, but they also participate in the carcinogenesis processes[22-24]. Thus, evaluating inflammatory smears is important.

In the literature, inflammatory cells are often related to lower genital tract infections including BV, Tv, Chlamydiasis, and fungal infections[19,26]. Notably, BV was diagnosed more commonly in patients with inflammation; however, 71% of patients with inflammatory Pap-tests showed no evidence of any specific microorganisms[6]. Specific infections including BV, fungal infection, Actinomycosis, Tv, and epithelial cell abnormalities were excluded from the cohort due to their possible effects on the gynecological complaints. In this study, inflammation was detected in 115 of 854 cases (13.5%) that had no other infections or abnormal epithelial cells.

The leukocyte count was used as a marker of inflammation in different tissues, and PMNLs counts "greater than 40" were considered inflammation in this study[27-30]. Neutrophils were the most prominent PMNLs in inflammatory Pap-smears. These cells contain a nucleus divided into 2–5 lobes and neutral granules. Neutrophil leukocytes were seen in almost all smears especially in patients who were pregnant or who had inflammation[31]. As seen in Figure 1b, some epithelial cells were entirely covered by neutrophils. Therefore, inflammatory smears should be evaluated carefully to avoid missing premalignant changes[32].

In this study, apoptotic PMNLs were frequently detected in the inflammatory background. Neutrophils are the most abundant PMNLs and first cells migrated to the inflammatory sites[12]. However, during inflammation, neutrophils are exposed for extended periods to multiple factors such as cytokines, chemokines, growth factors, and products of microorganisms[33]. Thus, increased apoptotic PMNLs may be related to prolonged exposure of cytokines and chemokines depending on inflammation process.

In this study, increased numbers of macrophages were also seen in patients with inflamed Pap-smears. Consistent with our results, increased numbers of cervical intraepithelial macrophages were found in inflammatory cervical smears[17]. The local influx of macrophages in the inflamed cervical epithelium may be related to the repair process of the epithelium as well as to inflammation[17].

In this study, eosinophil leukocytes and lymphocytes were seen to be less common compared to neutrophils and macrophages. Increased numbers of eosinophils called "eosinophilia" are linked to allergic, autoimmune, and infectious diseases as well as cancers[34]. Lymphocytes migrate to the vaginal epithelium during the luteal phase of menstrual cycle[34]. These cells are also related to chronic inflammation[31].

Vaginal discharge is secreted from glands in the vagina and cervix. Generally, women have vaginal discharge without an odor; it is composed of mucus, epithelial cells, and bacteria[32]. The main causes of abnormal vaginal discharge are BV, Tv, and Candidiasis[10]. The etiology of abnormal vaginal discharge can be defined by the imbalance of vaginal flora with pH changes[35]. In this study, the presence of vaginal discharge was statistically more frequent in women who had inflammatory changes (56.5%) compared to the control group (25.9%). The local influx of cytokines and the consequence of the increase of immune cells might be the reason for increased levels of vaginal discharge in patients with inflammation.

Vaginal discharge varies in color from transparent to white, yellow, yellowish-green, brown, and grey. The

color of discharge differs depend on the condition of the vagina. Yellowish color of vaginal discharge with fishy odor is a common complaint of BV[13], however white cheesy discharge is usually related to fungal infection[12]. Compared to the control group, vaginal discharge with grey and yellowish-green color were more frequently observed in patients with inflammatory smears.

There are several studies show the properties of inflammatory smears in the literature, however, in reflecting on this study, its key strength was the demonstration of the link between inflammation (without specific infectious agents and abnormal cells) and gynecological complaints for the first time. On the other hand, its findings are limited by the relatively small number of patients.

In conclusion, vaginal discharge is significantly more frequent in women suffering from inflammatory changes at their cervicovaginal smears. Moreover, increased levels of vaginal discharge in patients with inflammatory smears may be related to a local influx of cytokines. Inflammatory smears should be monitored more carefully to avoid missing premalignant changes. In further studies, immunocytochemical markers for chronic inflammation may be investigated in inflamed smears due to its close relationship with carcinogenesis.

**Yazar Katkıları:** Çalışma konsepti/Tasarımı: HGD, MSB; Veri toplama: HGD; Veri analizi ve yorumlama: HGD, MSB; Yazı taslağı: HGD; İçeriğin eleştirel incelenmesi: HGD, MSB; Son onay ve sorumluluk: HGD, MSB; Teknik ve malzeme desteği: HGD; Süpervizyon: HGD, MSB; Fon sağlama (mevcut ise): yok.
**Etik Onay:** Bu çalışma Hacettepe Üniversitesi Etik Kurulu tarafından onaylanmıştır (referans numarası GO18 / 915-34). Bu çalışmaya dahil olan tüm bireysel katılımcılardan yazılı bilgilendirilmiş onam alınmıştır.
**Hakem Değerlendirmesi:** Dış bağımsız.
**Çıkar Çatışması:** Yazarlar çıkar çatışması beyan etmemişlerdir.
**Finansal Destek:** Yazarlar finansal destek beyan etmemişlerdir.

**Author Contributions:** Concept/Design : HGD, MSB; Data acquisition: HGD; Data analysis and interpretation: HGD, MSB; Drafting manuscript: HGD; Critical revision of manuscript: HGD, MSB; Final approval and accountability: HGD, MSB; Technical or material support: HGD; Supervision: HGD, MSB; Securing funding (if available): n/a.
**Ethical Approval:** This study was approved by the Hacettepe University Ethics Committee (reference number GO18/915-34). Written informed consent was obtained from all individual participants included in this study.
**Peer-review:** Externally peer-reviewed.
**Conflict of Interest:** Authors declared no conflict of interest.
**Financial Disclosure:** Authors declared no financial support

## REFERENCES

1. Eckert LO, Koutsky LA, Kiviat NB, Krone MR, Stevens CE, Eschenbach DA. The inflammatory papanicolaou smear: What does it mean? Obstet Gynecol. 1995;86:360-6.
2. Beghini J, Giraldo PC, Eleutério J, Amaral RL do, Polpeta NC, Gonçalves AK. Vaginal inflammation: Association between leukocyte concentration and levels of immune mediators. Am J Reprod Immunol. 2016;75:126-33.
3. Fernandes JV, DE Medeiros Fernandes TA, DE Azevedo JC, Cobucci RN, DE Carvalho MG, Andrade VS et al. Link between chronic inflammation and human papillomavirus-induced carcinogenesis (Review). Oncol Lett. 2015;9:1015-26.
4. Baka S, Tsirmpa I, Chasiakou A, Tsouma I, Politi E, Gennimata V et al. Inflammation on the cervical papanicolaou smear: evidence for infection in asymptomatic women? Infect Dis Obstet Gynecol. 2013;2013:184302.
5. Ayres de Campos D, Nogueira A, Magalhães F, Bayer P, Monteiro J, Lameirão A et al. Células inflamatórias na citologia cervicovaginal. Um achado tradutor de infecção? [Inflammatory smears in cervicovaginal cytology. A finding meaning infection?]. Acta Med Port. 1997;10:637-41.
6. Bertolino JG, Rangel JE, Blake RL Jr, Silverstein D, Ingram E. Inflammation on the cervical papanicolaou smear: The predictive value for infection in asymptomatic women. Fam Med. 1992;24:447-52.
7. Anderson MR, Klink K, Cohrssen A. Evaluation of vaginal complaints. JAMA. 2004;291:1368-79.
8. von Glehn MP, Sidon LU, Machado ER. Gynecological complaints and their associated factors among women in a family health-care clinic. J Family Med Prim Care. 2017;6:88-92.
9. Spence D, Melville C. Vaginal discharge. BMJ. 2007;335:1147-51.
10. Schwebke JR. Vaginal Discharge In: Jeffrey D. Klausner, MD, Edward W. Hook III, MD, editors. Current diagnosis and treatment of sexually transmitted diseases. New York: McGraw-Hill Medical; 2007.
11. Hammond R. Gynaecological causes of abdominal pain. Women's Health Medicine. 2006;3:124-7.
12. Demirezen S, Dönmez HG, Özcan D, Beksaç MS. Evaluation of the relationship between fungal infection, neutrophil leukocytes and macrophages in cervicovaginal smears: Light microscopic examination. J Cytol. 2015;32:79-84.
13. Işik G, Demirezen Ş, Dönmez HG, Beksaç MS. Bacterial vaginosis in association with spontaneous abortion and recurrent pregnancy losses. J Cytol. 2016;33:135-140.
14. Lara-Torre E, Pinkerton JS. Accuracy of detection of trichomonas vaginalis organisms on a liquid-based papanicolaou smear. Am J Obstet Gynecol. 2003;188:354-6.
15. Merki-Feld GS, Lebeda E, Hogg B, Keller PJ. The incidence of actinomyces-like organisms in Papanicolaou-stained smears of copper- and levonorgestrel-releasing intrauterine devices. Contraception. 2000;61:365-8.

16. Nayar R, Wilbur DC. The Pap test and Bethesda 2014. Cancer Cytopathol. 2015;123:271-81.
17. Prakash M, Patterson S, Kapembwa MS. Macrophages are increased in cervical epithelium of women with cervicitis. Sex Transm Infect. 2001;77:366-9.
18. Dönmez HG, Demirezen Ş, Beksaç MS. Detection of the Wnt/Beta-catenin signaling activity by using immunocytochemical technique in cervical smears. Gynecol Obstet Reprod Med. 2013;19(2):91-5.
19. Barouti E, Farzaneh F, Sene AA, Tajik Z, Jafari B. The pathogenic microorganisms in Papanicolaou vaginal smears and correlation with inflammation. J Family Reprod Health. 2013;7:23-7.
20. Gami N, Trivedi S, Bhutia K, Puri M, Aggarwal K. Persistent inflammation on Pap smear: Does it warrant evaluation? Indian J Cancer. 2011;48:220.
21. Capaldo CT, Nusrat A. Cytokine regulation of tight junctions. Biochim Biophys Acta. 2009;1788:864-71.
22. Barrios De Tomasi J, Opata MM, Mowa CN. Immunity in the cervix: Interphase between immune and cervical epithelial cells. J Immunol Res. 2019;2019:7693183.
23. Förster C. Tight junctions and the modulation of barrier function in disease. Histochem Cell Biol. 2008;130:55-70.
24. Kobielak A, Boddupally K. Junctions and inflammation in the skin. Cell Commun Adhes. 2014;21:141-7.
25. Barouti E, Farzaneh F, Sene AA, Tajik Z, Jafari B. The pathogenic microorganisms in Papanicolaou vaginal smears and correlation with inflammation. J Family Reprod Health. 2013;7:23-7.
26. Verma A, Verma S, Vashist S, Attri S, Singhal A. A study on cervical cancer screening in symptomatic women using Pap smear in a tertiary care hospital in rural area of Himachal Pradesh, India. Middle East Fertil Soc J. 2017;22:39-42.
27. Kounis NG, Soufras GD, Tsigkas G, Hahalis G. White blood cell counts, leukocyte ratios, and eosinophils as inflammatory markers in patients with coronary artery disease. Clin Appl Thromb Hemost. 2015;21:139-43.
28. Randjelovic I, Moghaddam A, Freiesleben de Blasio B, Moi H. The role of polymorphonuclear leukocyte counts from urethra, cervix, and vaginal wet mount in diagnosis of nongonococcal lower genital tract infection. Infect Dis Obstet Gynecol. 2018;2018:8236575.
29. Madendag Y, Sahin E, Aydin E, Col Madendag I, Acmaz G, Karaman H. Neutrophil to lymphocyte ratio and platelet to lymphocyte ratio can be useful markers for distinguishing uterine adenomyosis and leiomyoma. Gynecol Obstet Reprod Med. 2018;24:147.
30. Mertoglu C, Gunay M, Gungor M, Kulhan M, Kulhan NG. A Study of inflammatory markers in gestational diabetes mellitus. Gynecol Obstet Reprod Med. 2018;25:1.
31. Boon ME, Suurmeijer AJH. The Pap Smear. 3rd ed. London: Harvard Academic Publishers; 1996.
32. Dasari P, Rajathi S, Kumar SV. Colposcopic evaluation of cervix with persistent inflammatory Pap smear: A prospective analytical study. Cytojournal. 2010;7:16.
33. Chakravarti A, Rusu D, Flamand N, Borgeat P, Poubelle PE. Reprogramming of a subpopulation of human blood neutrophils by prolonged exposure to cytokines. Lab Investig. 2009;89:1084-99.
34. Kurose N, Mizuguchi S, Ohkanemasa Y, Yamashita M, Nakano M, Guo X, Aikawa A, Nakada S, Sasagawa T, Yamada S. Adenosquamous carcinoma of the uterine cervix displaying tumor-associated tissue eosinophilia. SAGE Open Med Case Rep. 2019;7:2050313X19828235.
35. Lam KK, Simonds JL, Archer C, Ditzel AK, Wall S, Goyal V et al. Gynecological and obstetric emergencies. In: Borhart J, Bavolek R, editors. Essential Emergency Medicine. Philadelphia: Elsevier Inc.; 2007:497-554.