

Clinicopathologic significance of Papanicolaou smear study of postmenopausal women in a rural tertiary care center

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ABSTRACT

Background: Cervical cancer is a preventable disease in the vast majority of women. Papanicolaou (Pap) smear is still the most effective screening tool available for preventing cervical cancer. Therefore, it is important to investigate the significance of screening in older women. **Objective:** To study the distribution of cervical cancer among postmenopausal women and to determine the significance of cervical cancer screening in symptomatic and asymptomatic postmenopausal women. **Materials and Methods:** A total of 590 Pap smears were obtained from postmenopausal women between September 2012 and March 2013. Prefixed conventional cervical smears were stained with Pap stain. The cytology results were reported using the Bethesda system terminology. **Results:** Among the 590 postmenopausal women studied, 38.9% of asymptomatic postmenopausal women had clinically significant lesion whereas only 33.1% of symptomatic women had clinically significant lesion. There was low-grade squamous intraepithelial lesion at percentage of 17.5. Asymptomatic and symptomatic were 11.5% and 6.5%, respectively. High-grade squamous intraepithelial lesion was 4.5%. Asymptomatic and symptomatic were 7.5% and 2.85%, respectively. Atypical squamous cells of undetermined significance were seen in 8.85%. Asymptomatic and symptomatic were 4.25% and 4.6% respectively. Atypical glandular cells of undetermined significance were 1.7%. Only 3.2% of significant lesion was squamous cell carcinoma, and all were symptomatic. **Conclusion:** Postmenopausal women especially from the rural area and low socioeconomic strata suffered disproportionately from precancerous and cancerous lesions of the cervix. To reduce this burden, it's mandatory to motivate and screen asymptomatic older women.

Key words: Papanicolaou smear, postmenopause, squamous intraepithelial lesion, the Bethesda system

INTRODUCTION

Papanicolaou (Pap) and Traut reported the use of exfoliative cytology for the diagnosis of cervical cancer and precancerous lesions.^[1] Globally, cervical cancer is one of the most common cancers in women, with an estimate of 440,000 new cases annually. Eighty percent of these cases occurred in developing and undeveloped countries.^[2] According to 2008 estimates, invasive cervical cancer is the third most common cancer in women worldwide.^[3]

Median age of diagnosis is 52.2 years, and age distribution is bimodal, 35–39 and 60–64 years.^[4]

Cervical cancer is the most common cancer among women in sub-Saharan Africa, South Asia and Latin America, where 60% of all cases in the world occur.^[5] India accounts for one-fifth of the world burden of cervical cancer. Cervical cancer remained largely uncontrolled in high-risk developing countries because of ineffective or lack of screening program. Cervical cancer rate was still too high, particularly in the rural areas.^[6] In India, there was estimate more than 140,000 cases/year.^[7] Cervical cancer is the only gynecological cancer that met the WHO criteria for implementation of a screening program.^[8]

In India, there are no organized or high-level opportunistic screening programs for cervical cancer. Data from population-based cancer registry in different regions indicated a slow, but steady, decline in the incidence of

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cervical cancer. The absolute number of cases was increased due to population growth.^[6] Literature search yielded a very few studies done solely on postmenopausal women.^[9,10] Therefore, the objective of this study was to assess the significance of screening in postmenopausal rural women. We included women attending rural camps in and around our institution.

MATERIALS AND METHODS

The study was conducted at Pathology Department, Sri Manakula Vinayagar Medical College for 6 months duration between September 2012 and March 2013. Cytological specimens from postmenopausal women were collected from Department of Gynecology and camps conducted in the rural areas in and around the college locality.

Cytological specimens were collected by trained technician in camps and by gynecologist in women attending outpatient department in the hospital. Women were advised not to use douching, vaginal creams or jellies for 48 h before the collection. They were placed in modified lithotomy position after taking consent in screening camps and hospital. Cervix was exposed using bivalve vaginal speculum. Ayre’s spatula was placed at the cervical os and gently rotated 360° twice to obtain a scraping of the cervical cells. Cervical smear was prepared by uniformly spreading the specimen across a glass slide. It was immediately fixed in 95% ethyl alcohol contained in a Coplin jar and transported to the cytology laboratory. Conventional Pap smear were stained with modified Pap stain and reported according to the Bethesda system 2001 terminology.^[11] All the smears were conventional Pap smear and examined by two experienced cytopathologists. Cytological abnormalities was defined by one of the terminology: Atypical squamous cells of undetermined significance (ASCUS), atypical glandular cells of undetermined significance (AGUS), low-grade squamous intraepithelial lesion (LSIL), high-grade squamous intraepithelial lesions (HSIL), squamous cell carcinoma (SCC) and adenocarcinoma. Collected data from the predesigned proforma was entered into Statistical Package for Social Sciences version 10.0, (USA) analyzed descriptively and represented by bar chart.

RESULTS

Study subjects

A total of 610 women were screened. Of the women screened, 20 had inadequacy specimens for evaluation and were excluded. Overall, 590 women were taken into account for analysis. Most of the women were asymptomatic (45.8%). Others presented with clinical history of uterine prolapse (22.9%), postmenopausal

bleeding (14.4%), white discharge (9.3%) and white discharge with cervical erosion on examination (7.6%).

The age distribution is presented in Table 1. All the cases had never undergone cervical cancer screening before. All of them were multiparous and classified as low and low-middle income group. The spectrum of cytological changes noted in 590 smears was depicted in the bar chart.

Results of cytology screening

Out of 270 (45.8%) smears taken from asymptomatic postmenopausal women, insignificant cytological findings were noted in 165 (28%). Of which, atrophy was commonest found in 80 cases (13.5%) followed by nonspecific inflammation (7.6%), metaplasia (4.2%), *Trichomonas vaginalis* (1.7%) and herpes simplex virus changes (0.85%). Abnormal cytological findings were seen in 105 (17.8%). Of which, majority of them had LSIL 65 (11%) followed by ASCUS 25 (4.25%), HSIL 10 (1.7%) and AGUS 5 (0.85%). There was no cancer cases in this study. The percentage of LSIL was higher in asymptomatic women than in symptomatic women. Significant number of smears had ASCUS Figure 1.

Among 135 (22.9%) smears taken from women with uterine prolapse, 99 (16.8%) were insignificant, and 36 (6.1%) showed significant changes. LSIL was 4.1%. HSIL was

Table 1: Age distribution of symptomatic and asymptomatic postmenopausal women

Age in years	Number of cases
40-49	200
50-59	280
60-69	70
70 and above	40
Total	590

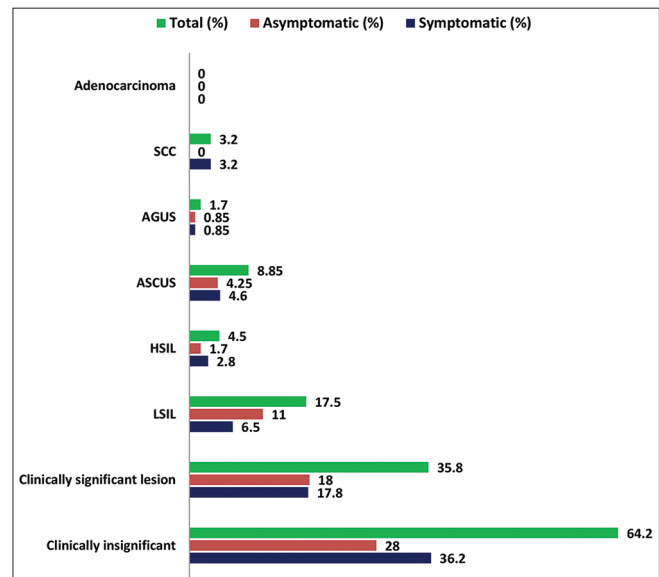


Figure 1: Chart showing total symptomatic and asymptomatic case percentages

2%. Women with uterine prolapse contributed the highest number of total HSIL cases.

Among 85 (14.4%) women with postmenopausal bleeding, 45 (7.6%) cases had insignificant changes and 40 (6.8%) cases had abnormal findings. LSIL, ASCUS, SCC, AGUS and HSIL were found in 14 (2.4%), 10 (1.7%), 6 (1%), 5 (0.85%) and 5 (0.85%) cases respectively. Equal number of AGUS was seen in asymptomatic and postmenopausal women with bleeding.

Out of 55 (9.3%) smears taken from women with postmenopausal white discharge, 35 (5.9%) and 20 (3.4%) cases had insignificant and significant change, respectively. Of 20 (3.4%) abnormal findings, ASCUS and SCC was found in 13 (2.2%) and 7 (1.2%) cases, respectively. The highest percentage of SCC was seen in this group.

Among 45 (7.6%) women with white discharge and cervical erosion on examination, 35 (5.9%) had insignificant findings and abnormal findings was seen in 10 (1.7%). Of which, SCC was seen in 6 (1%) cases followed by 4 (0.7%) ASCUS cases.

To summarize, 38.9% of asymptomatic postmenopausal women had clinically significant lesion whereas only 33.1% of symptomatic women had clinically significant lesion. LSIL was found at the percentage of 17.5%, 11% and 6.5% of them asymptomatic and symptomatic, respectively. HSIL was found at percentage of 4.5, 1.7% and 2.85% of cases were symptomatic and symptomatic, respectively. ASCUS was seen in 8.85%, 4.25% and 4.6% were asymptomatic and symptomatic, respectively. There was only 1.7% of AGUS, 0.85% of cases were seen in symptomatic and asymptomatic women. Only 3.2% of significant lesion was SCC, and all of them were symptomatic [Table 2].

DISCUSSION

Study institute located around 22 km away from the city and was surrounded by rural population. The routine gynecological examination and Pap smear examination were

offered free of cost. The study found that women were poorly aware of the indications and benefits of cervical cancer screening after menopause. Awareness about the Pap test was absent in our study population, none had a Pap test done previously. Many believed that Pap smear was performed only on women who were symptomatic and perceived themselves as not at risk of developing cervical cancer. Many thought that the purpose of a Pap smear test was to detect the existing cervical cancer. Such misconceptions required extensive public education, with a new emphasis on the crucial fact that Pap smear screening was targeted primarily at detecting the precursor lesions that occurred early in the course of the disease. Subsequent timely treatment would thus impede progress toward invasive cancer. This concurred with many other studies.^[12-14]

Uterine prolapsed, abnormal vaginal discharge and postmenopausal bleeding were the commonest presentation among our women and the majority of them who had neoplastic lesions were in the age-group of 50–59 years. Early marriage, low income and multiparity were the common risk factors seen in study population. This was comparable to the study conducted by Engelstad *et al.*, which showed that low-income women were at higher risk of developing cervical cancer.^[15]

Recent studies suggested the cervical cancer increased in older age group.^[3] We studied Pap smears of 610 postmenopausal females. Out of which 590 smears were adequate for reporting. Only 3.2% of smears were inadequate for reporting, the proportion of inadequate smears ranged from 0.2–5% in other studies.^[16-20]

Misra and Singh did a long term urban hospital-based screening in asymptomatic women and found precancerous and cancerous lesions of the cervix in 5.9% and 0.6%, respectively.^[21] In this study, only symptomatic women had malignancy. Gupta *et al.* did a population-based study in Western Uttar Pradesh and found precancerous lesion of the cervix in 2.27% of cases and a relatively high prevalence with increasing age.^[22] Mulay *et al.* conducted urban hospital and population-based study in India and Mauritius. They found that 1.4% and 0.47% precancerous lesion in India and Mauritian group, respectively.^[23]

In present study, precancerous lesion was seen in 12.7% of asymptomatic women that is more than twice the urban population study. Findings of our study can be compared to Bukhari *et al.* study and other studies conducted in a rural population except for few variations.^[24] Bukhari *et al.* study included 67% of postmenopausal women and around 50% smears were normal. Of the 102 cases with neoplastic lesions 46 patients (45%) had LSIL Figure 2, HSIL Figure 3, SCC Figure 4 and adenocarcinoma in 22 (21.5%), 14 (13.7%)

Table 2: Summary of result noted on Pap smear in postmenopausal women

	Symptomatic	Asymptomatic	Total
Clinically insignificant	36.2	28	64.2
Clinically significant lesion	17.8	18	35.8
LSIL	6.5	11	17.5
HSIL	2.8	1.7	4.5
ASCUS	4.6	4.25	8.85
AGUS	0.85	0.85	1.7
SCC	3.2	0	3.2
Adenocarcinoma	0	0	0

LSIL: Low-grade squamous intraepithelial lesion, HSIL: High-grade squamous intraepithelial lesion, ASCUS: Atypical squamous cells of undetermined significance, AGUS: Atypical glandular cells of undetermined significance, SCC: Squamous cell carcinoma, Pap: Papanicolaou

and 6 (5.8%) cases, respectively. Ten (9.8%) cases showed cytology of ASCUS and 4 (3.9%) cases had AGUS. However, we did not come across adenocarcinoma on cytology. Five of asymptomatic postmenopausal women in our study had benign endometrial cells Figure 5. These women were further evaluated for endometrial pathology as suggested by Ashfaq *et al.* study in which 39% of postmenopausal women with benign endometrial cells on cytology had endometrial pathology.^[25] The Bethesda system recommends the use of ASCUS when the abnormalities seen in squamous cells are too pronounced to be attributed solely to reactive changes, but the changes are not enough to be categorized as squamous intraepithelial lesion.^[11] ASCUS was a broad diagnostic category that could be attributed to human papillomavirus infection (HPV), malignant neoplasia and reactive conditions.^[24] There was 8.85% of ASCUS in the present study. Although, the risk of developing malignant neoplasia was low in elderly women, but still need to follow-up.^[26] HPV change was found at percentage of 8.5% in LSIL. Recent study in women 50 years and older suggest,

a positive high-risk HPV test resulted significantly increased the likelihood of follow-up histopathologic diagnoses of cervical intraepithelial neoplasia 2/3 or more in patients with HSIL, LSIL, and ASC-H Pap test results compared to women with negative high-risk HPV test results.^[27] Increasing the use of routine Pap and HPV cotesting in elderly women could decrease the burden of cancer in India. Glandular atypical in Pap smears from postmenopausal women was frequently encountered. The diagnostic category of AGUS denoted cytologic changes in endocervical or endometrial cells that exceed those typical of reactive changes but are quantitatively and/or qualitatively not diagnostic of adenocarcinoma.^[11] Chhieng *et al.* did a study on postmenopausal women with AGUS (0.51% incidence) on cytology and found clinically significant lesion in 32.7% of AGUS on subsequent histologic follow-up. This study strongly suggested the need for close follow-up of postmenopausal patients with a diagnosis of AGUS.^[9] Prevalence of epithelial abnormalities around the world showed wide variation from 0.98% to 15.5%.^[28,29] This could result from the variation in criteria, intra

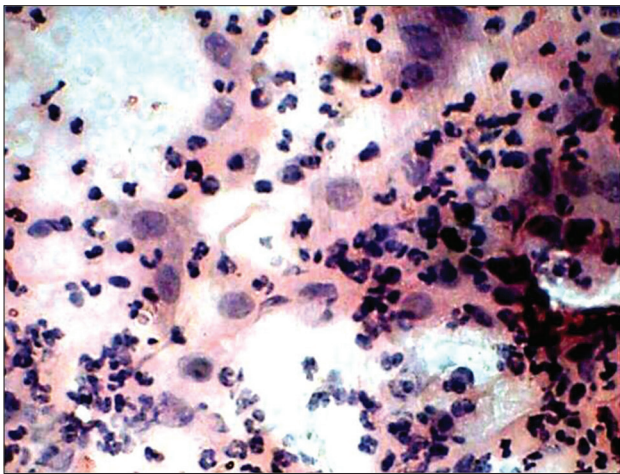


Figure 2: Photomicrograph of cervical smear showing low-grade squamous intraepithelial lesion, (Papanicolaou, x40)

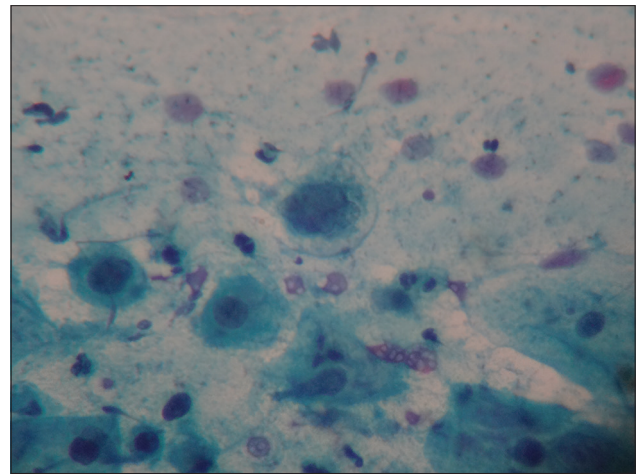


Figure 3: Photomicrograph of cervical smear showing high-grade squamous intraepithelial lesion, (Papanicolaou, x40)

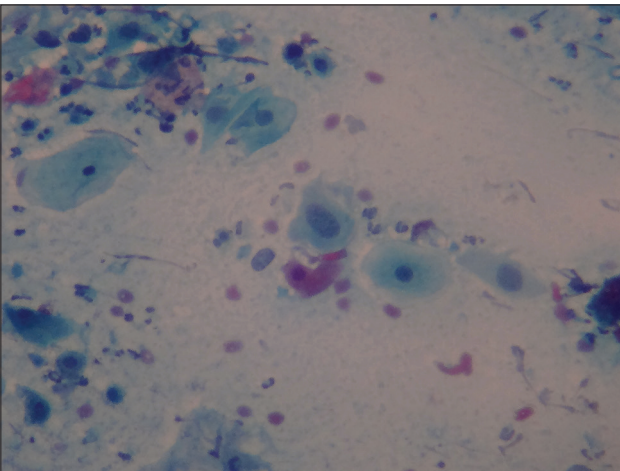


Figure 4: Photomicrograph of cervical smear showing squamous cell carcinoma, (Papanicolaou, x40)

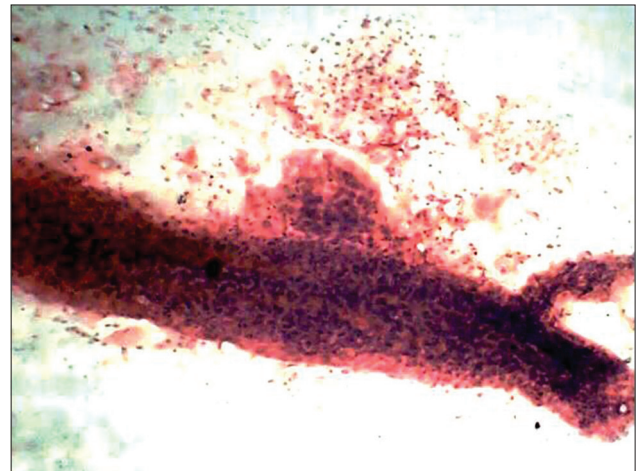


Figure 5: Photomicrograph of cervical smear showing endometrial cells, (Papanicolaou, x10)

and interobserver variation, differences in the population studied and sample size. So it became extremely difficult to do a comparative study.

CONCLUSION

Papanicolaou smear was a valuable investigation tool for a screening procedure in postmenopausal women. It was recommended that reporting should be followed by the Bethesda system as it improved the reproducibility and helped in the identification of ASCUS and AGUS lesions. It also played a key role to diagnose various intraepithelial lesions and invasive lesions at an early stage and manage them properly. Postmenopausal women especially from rural areas and from low socioeconomic groups suffered disproportionately from precancerous and cancerous lesions of the cervix. The incidence of HPV infection was much higher in rural areas than estimated since most of the cases in our study were asymptomatic. Motivation of postmenopausal women by media and implementation of health awareness program by Government in the form of screening rural women and thorough investigation and follow-up of women with abnormal Pap smear can reduce the burden of cervical cancer.

REFERENCES

- Papanicolaou GN, Traut HF. The diagnostic value of vaginal smears in carcinoma of the uterus 1941. *Arch Pathol Lab Med* 1997;121:211-24.
- Masood S. A plea for a worldwide volunteer cervical cancer education and awareness program. A proposal from the International Academy of Cytology Committee on Cancer Detection for Medically Underserved Women. *Acta Cytol* 1999;43:539-43.
- Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer* 2010;127:2893-917.
- Fakhrjou A, Dastranj-Tabrizi A, Ghojzadeh M, Ghorashi S, Velayati A, Piri R, et al. Diagnostic value of protein Ki67 (MIB-1) in atypical pap smears of postmenopausal women. *Asian Pac J Cancer Prev* 2013;14:4815-8.
- Parkin DM, Bray FI, Devesa SS. Cancer burden in the year 2000. The global picture. *Eur J Cancer* 2001;37 Suppl 8:S4-66.
- Sankaranarayanan R, Budukh AM, Rajkumar R. Effective screening programmes for cervical cancer in low- and middle-income developing countries. *Bull World Health Organ* 2001;79:954-62.
- Juneja A, Sehgal A, Sharma S, Pandey A. Cervical cancer screening in India: Strategies revisited. *Indian J Med Sci* 2007;61:34-47.
- Rajendra AK, Yogesh VK. Screening for cervical cancer: An overview. *J Obstet Gynecol India* 2006;56:115-22.
- Gyllensten U, Gustavsson I, Lindell M, Wilander E. Primary high-risk HPV screening for cervical cancer in post-menopausal women. *Gynecol Oncol* 2012;125:343-5.
- Chhieng DC, Elgert P, Cohen JM, Cangiarella JF. Clinical significance of atypical glandular cells of undetermined significance in postmenopausal women. *Cancer* 2001;93:1-7.
- Solomon D, Davey D, Kurman R, Moriarty A, O'Connor D, Prey M, et al. The 2001 Bethesda System: Terminology for reporting results of cervical cytology. *JAMA* 2002;287:2114-9.
- Breitkopf CR, Pearson HC, Breitkopf DM. Poor knowledge regarding the Pap test among low-income women undergoing routine screening. *Perspect Sex Reprod Health* 2005;37:78-84.
- Holroyd E, Twinn S, Adab P. Socio-cultural influences on Chinese women's attendance for cervical screening. *J Adv Nurs* 2004;46:42-52.
- Wong LP, Wong YL, Low WY, Khoo EM, Shuib R. Knowledge and awareness of cervical cancer and screening among Malaysian women who have never had a Pap smear: A qualitative study. *Singapore Med J* 2009;50:49-53.
- Engelstad LP, Stewart SL, Nguyen BH, Bedeian KL, Rubin MM, Pasick RJ, et al. Abnormal Pap smear follow-up in a high-risk population. *Cancer Epidemiol Biomarkers Prev* 2001;10:1015-20.
- Pan Q, Belinson JL, Li L, Pretorius RG, Qiao YL, Zhang WH, et al. A thin-layer, liquid-based pap test for mass screening in an area of China with a high incidence of cervical carcinoma. A cross-sectional, comparative study. *Acta Cytol* 2003;47:45-50.
- Tuncer ZS, Basaran M, Sezgin Y, Firat P, Mocan Kuzey G. Clinical results of a split sample liquid-based cytology (ThinPrep) study of 4,322 patients in a Turkish institution. *Eur J Gynaecol Oncol* 2005;26:646-8.
- Kapila K, George SS, Al-Shaheen A, Al-Ottibi MS, Pathan SK, Sheikh ZA, et al. Changing spectrum of squamous cell abnormalities observed on papanicolaou smears in Mubarak Al-Kabeer Hospital, Kuwait, over a 13-year period. *Med Princ Pract* 2006;15:253-9.
- Insinga RP, Glass AG, Rush BB. Diagnoses and outcomes in cervical cancer screening: A population-based study. *Am J Obstet Gynecol* 2004;191:105-13.
- Fonn S, Bloch B, Mabina M, Carpenter S, Cronje H, Maise C, et al. Prevalence of pre-cancerous lesions and cervical cancer in South Africa – A multicentre study. *S Afr Med J* 2002;92:148-56.
- Misra JS, Singh U. Results of longterm hospital based cytological screening in asymptomatic women. *Diagn Cytopathol* 2006;34:184-7.
- Gupta K, Malik NP, Sharma VK, Verma N, Gupta A. Prevalence of cervical dysplasia in western Uttar Pradesh. *J Cytol* 2013;30:257-62.
- Mulay K, Swain M, Patra S, Gowrishankar S. A comparative study of cervical smears in an urban Hospital in India and a population-based screening program in Mauritius. *Indian J Pathol Microbiol* 2009;52:34-7.
- Bukhari MH, Saba K, Qamar S, Majeed MM, Niazi S, Naeem S. Clinicopathological importance of Papanicolaou smears for the diagnosis of premalignant and malignant lesions of the cervix. *J Cytol* 2012;29:20-5.
- Ashfaq R, Sharma S, Dullely T, Saboorian MH, Siddiqui MT, Warner C. Clinical relevance of benign endometrial cells in postmenopausal women. *Diagn Cytopathol* 2001;25:235-8.
- Rodriguez EF, Reynolds JP, Jenkins SM, Winter SM, Henry MR, Nassar A. Atypical squamous cells of undetermined significance in patients with HPV positive DNA testing and correlation with disease progression by age group: An institutional experience. *Int J Clin Exp Pathol* 2012;5:428-35.
- Zhao C, Zhao S, Heider A, Austin RM. Significance of high-risk human papillomavirus DNA detection in women 50 years and older with squamous cell papanicolaou test abnormalities. *Arch Pathol Lab Med* 2010;134:1130-5.
- Sadan O, Schejter E, Ginath S, Bachar R, Boaz M, Menczer J, et al. Premalignant lesions of the uterine cervix in a large cohort of Israeli Jewish women. *Arch Gynecol Obstet* 2004;269:188-91.
- Thistle PJ, Chirenje ZM. Cervical cancer screening in a rural population of Zimbabwe. *Cent Afr J Med* 1997;43:246-51.

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