

Comparative Analysis of Cervical Cytological Findings in Premenopausal and Postmenopausal Women Using Liquid-Based Cytology: A Retrospective Study from a Tertiary Care Center

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ABSTRACT **Background:** Cervical cancer remains a major cause of cancer-related morbidity and mortality among women worldwide, particularly in low- and middle-income countries where screening coverage remains suboptimal. Cervical cytology plays a pivotal role in the early detection of premalignant and malignant cervical lesions. Hormonal and physiological changes associated with menopause significantly influence cervical cytomorphology and may affect the spectrum of cytological findings.

Aim: To analyze and compare the spectrum of cervical cytological findings in premenopausal and postmenopausal women undergoing cervical cancer screening at a tertiary care teaching hospital.

Materials and Methods: This retrospective observational comparative study was conducted in the Department of Pathology at Vydehi Institute of Medical Sciences and Research Centre, Bengaluru. A total of 762 cervical cytology samples were evaluated, of which 749 satisfactory smears were included in the final analysis. Cervical samples were processed using Liquid-Based Cytology (LBC) and interpreted according to The Bethesda System for Reporting Cervical Cytology (TBSRTC), 2014. Women were categorized into premenopausal and postmenopausal groups based on menopausal status. Comparative analysis was performed using the Chi-square test, and odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. A p-value of <0.05 was considered statistically significant.

Results: Of the 749 satisfactory smears, 439 (58.6%) were obtained from premenopausal women and 310 (41.4%) from postmenopausal women. Inflammatory smears were the most common cytological finding and were significantly more frequent among premenopausal women than postmenopausal women [240/439 (54.7%) vs. 98/310 (31.6%); $p < 0.001$]. Atrophic smears and atrophic smears with inflammation were significantly more common among postmenopausal women, accounting for 24.2% and 11.9% of cases, respectively ($p < 0.001$). Postmenopausal women demonstrated significantly increased odds of exhibiting atrophic smears (OR=8.44; 95% CI: 4.81–14.81) and atrophic smears with inflammation (OR=19.70; 95% CI: 6.01–64.51). Epithelial cell abnormalities were uncommon and accounted for only 0.7% of satisfactory smears. Two cases of ASC-US were identified among postmenopausal women, while isolated cases of LSIL, HSIL, and squamous cell carcinoma were observed in premenopausal women.

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Conclusion: Significant menopausal variation exists in cervical cytological patterns, with inflammatory lesions predominating among premenopausal women and atrophic alterations showing a strong association with postmenopausal status. Awareness of these age-related cytomorphological changes is essential for accurate interpretation of cervical smears and avoidance of diagnostic pitfalls. Liquid-Based Cytology provides high specimen adequacy and remains an effective screening modality for cervical cancer screening and early lesion detection in resource-limited settings.

Keywords: Cervical cytology; Pap smear; Liquid-based cytology; Premenopausal women; Postmenopausal women; Cervical cancer screening; Bethesda system; Cervical epithelial abnormalities

INTRODUCTION

Cervical cancer remains one of the leading causes of cancer-related morbidity and mortality among women worldwide and continues to pose a substantial public health challenge, particularly in low- and middle-income countries. According to recent GLOBOCAN 2024 estimates, cervical carcinoma remains among the most common gynecological malignancies globally, with a disproportionately higher disease burden in developing nations due to inadequate screening coverage, delayed diagnosis, poor socioeconomic conditions, and limited access to healthcare facilities [1]. Despite significant advances in preventive strategies, cervical cancer continues to account for considerable mortality in resource-constrained settings, highlighting the persistent need for effective and accessible screening programs. Persistent infection with high-risk human papillomavirus (HPV), especially HPV types 16 and 18, is recognized as the principal etiological factor in cervical carcinogenesis [2]. The prolonged premalignant phase of cervical intraepithelial neoplasia provides a critical window for early detection and intervention before progression to invasive carcinoma. Consequently, organized cervical cancer screening programs have significantly contributed to reductions in cervical cancer incidence and mortality in countries with established screening infrastructure [3].

Cervical cytology using the Papanicolaou (Pap) smear remains one of the most widely utilized screening modalities for the early detection of premalignant and malignant cervical lesions because of its simplicity, cost-effectiveness, and applicability in large-scale population screening [4]. In addition to identifying epithelial

abnormalities, cervical cytology also facilitates the detection of inflammatory, infectious, reactive, and atrophic cervical changes. Recent advances in Liquid-Based Cytology (LBC) have further improved specimen adequacy, cellular preservation, and background clarity while reducing obscuring inflammatory and hemorrhagic artifacts, thereby enhancing cytological interpretation and diagnostic accuracy [5].

Cervical cytomorphology is influenced by hormonal status and age-related physiological alterations. Premenopausal women frequently exhibit inflammatory and infectious lesions related to active reproductive physiology, whereas postmenopausal women commonly demonstrate atrophic cellular changes secondary to estrogen deficiency [6]. Atrophic smears often show predominance of parabasal cells, nuclear hyperchromasia, and degenerative alterations that may mimic squamous intraepithelial lesions, creating important diagnostic challenges in routine cytopathology practice. Furthermore, persistent HPV infection in postmenopausal women may exhibit delayed viral clearance and increased risk of progression to high-grade lesions due to age-related immunological changes [7].

Recent cervical cancer screening guidelines increasingly emphasize HPV-based screening and co-testing strategies, particularly in women above 30 years of age [3], [8]. However, cytology-based screening continues to play a major role in low-resource settings because of its accessibility and affordability. Comparative evaluation of cervical cytological findings between premenopausal and postmenopausal women is therefore clinically relevant for understanding age-related cytomorphological variations, avoiding interpretational pitfalls, and optimizing cervical cancer screening strategies. Although several studies have evaluated cervical cytology patterns in the general female population, relatively limited Indian studies have specifically compared the cytomorphological spectrum between premenopausal and postmenopausal women using Liquid-Based Cytology techniques. The present study was therefore undertaken to analyze and compare the spectrum of Pap smear findings in premenopausal and postmenopausal women attending a tertiary care teaching hospital, with particular emphasis on inflammatory, infectious, atrophic, and epithelial abnormalities and their clinicocytological correlations.

MATERIALS AND METHODS

Study Design and Setting

This retrospective observational comparative study was conducted in the Department of Pathology in collaboration with the Department of Obstetrics and Gynecology at Vydehi Institute of Medical Sciences and Research Centre, Bengaluru, India. The study aimed to evaluate and compare the spectrum of cervical cytological findings in premenopausal and postmenopausal women undergoing cervical cancer screening.

Study Duration

The study was carried out over a 12-month period from January 2025 to December 2025.

Study Population

The study population comprised women attending the gynecology outpatient department who underwent cervical cytology screening either as part of routine health evaluation or for gynecological complaints during the study period.

Sample Size and Study Groups

A total of 762 cervical cytology samples were retrieved and analyzed from departmental records. Of these, 749 smears were satisfactory for evaluation and included in the final analysis, while 13 smears were categorized as unsatisfactory according to Bethesda adequacy criteria.

The study population was stratified into two groups based on menopausal status:

- Premenopausal group: women aged 40–50 years
- Postmenopausal group: women aged >50 years

Among the satisfactory smears, 439 cases belonged to the premenopausal group and 310 cases belonged to the postmenopausal group.

Inclusion Criteria

1. Women aged 40 years and above undergoing Pap smear examination
2. Women presenting with symptoms such as vaginal discharge, lower abdominal pain, irregular menstrual bleeding, postmenopausal bleeding, or other gynecological complaints
3. Women undergoing routine cervical cancer screening
4. Adequate cervical cytology smears available for interpretation

Exclusion Criteria

1. Pregnant women
2. Women with active bleeding per vaginum at the time of sample collection
3. Women receiving hormone replacement therapy
4. Women with prior surgical or therapeutic intervention for cervical lesions
5. Repeat smears from the same patient during the study period
6. Unsatisfactory smears for detailed cytological evaluation

Sample Collection and Cytological Processing:

Cervical samples were collected by trained gynecologists under aseptic precautions using an Ayre's spatula and end cervical

brush. Samples were processed using the Liquid-Based Cytology (LBC) technique. The collected cellular material was immediately transferred into a liquid preservative medium to ensure optimal fixation and uniform cellular distribution.

Specimens were transported to the cytopathology laboratory and processed according to standard laboratory protocols. Thin-layer preparations were prepared and subsequently stained using the conventional Papanicolaou staining method.

Cytological Interpretation

All cervical smears were independently evaluated by experienced cytopathologists and reported according to The Bethesda System for Reporting Cervical Cytology (TBSRTC), 2014.

Smears were categorized into the following groups:

1. Negative for Intraepithelial Lesion or Malignancy (NILM)
 - Normal cytology
 - Inflammatory smears
 - Atrophic smears
 - Atrophic smears with inflammation
 - Infectious lesions including candidiasis, trichomans and bacterial vaginosis

Epithelial Cell Abnormalities

- Atypical Squamous Cells of Undetermined Significance (ASC-US)
- Low-grade Squamous Intraepithelial Lesion (LSIL)
- High-grade Squamous Intraepithelial Lesion (HSIL)
- Squamous Cell Carcinoma

Smears not fulfilling adequacy criteria were reported as unsatisfactory.

Clinical and Demographic Parameters

Relevant clinical and demographic details including age, menopausal status, presenting complaints and parity, were obtained from cytology requisition forms and hospital medical records.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) software version 21.0 (IBM Corp., Armonk, NY, USA).

Descriptive statistics were expressed as frequencies and percentages. Comparative analysis between premenopausal and postmenopausal groups was performed using the Chi-square test to determine statistical significance between categorical variables. A p-value of <0.05 was considered statistically significant [Tables 1-6].

Table 1: Smear Adequacy and Demographic Characteristics.

| Parameter | Premenopausal | Postmenopausal | Total |
|------------------------|---------------|----------------|-------|
| Satisfactory smears | 439 | 310 | 749 |
| Unsatisfactory smears | 13 | 0 | 13 |
| Total smears evaluated | 452 | 310 | 762 |
| Mean age (years) | 45.2 ± 3.1 | 58.6 ± 6.8 | - |

Table 2: Clinical Presentation of Patients.

| Clinical Symptom | Premenopausal n (%) | Postmenopausal n (%) | Total |
|--------------------------------|---------------------|----------------------|-------|
| Vaginal discharge | 248 (56.5) | 84 (27.1) | 332 |
| Lower abdominal pain | 102 (23.2) | 71 (22.9) | 173 |
| Irregular bleeding | 48 (10.9) | 26 (8.4) | 74 |
| Postmenopausal bleeding | 0 | 41 (13.2) | 41 |
| Routine screening/asymptomatic | 41 (9.3) | 88 (28.4) | 129 |
| Total | 439 | 310 | 749 |

Table 3: Distribution of Cervical Cytological Findings.

| Cytological Finding | Premenopausal n (%) | Postmenopausal n (%) | Total n (%) |
|----------------------------------|---------------------|----------------------|-------------|
| NILM | 161 (36.7) | 86 (27.7) | 247 (33.0) |
| Inflammatory smear | 240 (54.7) | 98 (31.6) | 338 (45.1) |
| Atrophic smear | 16 (3.6) | 75 (24.2) | 91 (12.1) |
| Atrophic smear with inflammation | 3 (0.7) | 37 (11.9) | 40 (5.3) |
| Candidiasis | 14 (3.2) | 12 (3.9) | 26 (3.5) |
| ASC-US | 0 | 2 (0.6) | 2 (0.3) |
| LSIL | 1 (0.2) | 0 | 1 (0.1) |
| HSIL | 1 (0.2) | 0 | 1 (0.1) |
| Squamous cell carcinoma | 1 (0.2) | 0 | 1 (0.1) |
| Radiation changes | 2 (0.5) | 0 | 2 (0.3) |
| Total | 439 | 310 | 749 |

Table 4: Association Between Menopausal Status and Cytological Findings.

| Cytological Finding | Odds Ratio (OR) | 95% CI | p-value |
|----------------------------------|-----------------|------------|---------|
| Atrophic smear | 8.44 | 4.81–14.81 | <0.001 |
| Atrophic smear with inflammation | 19.7 | 6.01–64.51 | <0.001 |
| Inflammatory smear | 0.38 | 0.28–0.52 | <0.001 |
| NILM | 0.66 | 0.48–0.91 | 0.01 |

Table 5: Distribution of Epithelial Cell Abnormalities.

| Epithelial Abnormality | Premenopausal | Postmenopausal | Total |
|-------------------------|---------------|----------------|-------|
| ASC-US | 0 | 2 | 2 |
| LSIL | 1 | 0 | 1 |
| HSIL | 1 | 0 | 1 |
| Squamous cell carcinoma | 1 | 0 | 1 |
| Total | 3 | 2 | 5 |

Table 6: Distribution of Infectious Lesions.

| Infectious Lesion | Premenopausal | Postmenopausal | Total |
|-----------------------|---------------|----------------|-------|
| Candidiasis | 14 | 12 | 26 |
| Trichomonas vaginalis | 7 | 0 | 7 |
| Bacterial vaginosis | 37 | 0 | 37 |
| Total | 58 | 12 | 70 |
| Total | 3 | 2 | 5 |

RESULTS

Study Population and Smear Adequacy

A total of 762 cervical cytology samples were evaluated during the study period. Of these, 749 (98.3%) smears were satisfactory for cytological interpretation, while 13 (1.7%) were categorized as unsatisfactory according to Bethesda adequacy criteria and excluded from further analysis. Among the satisfactory smears, 439 (58.6%) belonged to premenopausal women and 310 (41.4%) to postmenopausal women. The mean age of women in the premenopausal group was 45.2 ± 3.1 years, whereas the mean age in the postmenopausal group was 58.6 ± 6.8 years. All unsatisfactory smears were encountered in the premenopausal group.

Clinical Presentation

Vaginal discharge was the most common presenting complaint among premenopausal women, accounting for 248 (56.5%) cases, followed by lower abdominal pain in 102 (23.2%) cases and irregular bleeding in 48 (10.9%) cases. Among postmenopausal women, vaginal discharge was reported in 84 (27.1%) cases, while postmenopausal bleeding was observed in 41 (13.2%) cases. Routine cervical screening or evaluation in asymptomatic women was more common among postmenopausal women [88 (28.4%)] compared with premenopausal women [41 (9.3%)].

Spectrum of Cervical Cytological Findings

Inflammatory smears constituted the most frequent cytological finding and accounted for 338 of 749 satisfactory smears (45.1%). These were significantly more common among premenopausal women than postmenopausal women [240/439 (54.7%) versus 98/310 (31.6%); $p < 0.001$].

Atrophic cervical changes demonstrated a strong association with postmenopausal status. Atrophic smears were identified in 75 (24.2%) postmenopausal women compared with 16 (3.6%) premenopausal women ($p < 0.001$). Similarly, atrophic smears associated with inflammation were significantly more common among postmenopausal women [37 (11.9%)] than among premenopausal women [3 (0.7%)] ($p < 0.001$).

Negative for intraepithelial lesion or malignancy (NILM) was reported in 247 cases (33.0%), including 161 (36.7%) premenopausal and 86 (27.7%) postmenopausal women. Candidiasis was identified in 26 cases (3.5%), with a comparable distribution between the two groups.

Association between Menopausal Status and Cytological Findings

A significant association was observed between menopausal status and cervical cytological patterns. Postmenopausal women demonstrated significantly increased odds of exhibiting atrophic smears (OR=8.44; 95% CI: 4.81–14.81; $p < 0.001$). Likewise, atrophic smears with inflammation showed a strong association

with postmenopausal status (OR=19.70; 95% CI: 6.01–64.51; $p < 0.001$).

Conversely, inflammatory smears were less common among postmenopausal women (OR=0.38; 95% CI: 0.28–0.52; $p < 0.001$). NILM smears also demonstrated a lower prevalence among postmenopausal women (OR=0.66; 95% CI: 0.48–0.91; $p = 0.01$).

Epithelial Cell Abnormalities

Epithelial cell abnormalities were infrequent and accounted for only 5 of 749 satisfactory smears (0.7%). Two cases of ASC-US were identified, both occurring in postmenopausal women. Isolated cases of LSIL, HSIL, and squamous cell carcinoma were observed in the premenopausal group. No cases of LSIL, HSIL, or squamous cell carcinoma were detected among postmenopausal women.

Infectious Lesions

Among infectious lesions, candidiasis was the most frequently encountered fungal infection, accounting for 26 cases. Trichomonas vaginalis infection was identified in seven cases, all occurring in premenopausal women. Bacterial vaginosis was observed in 37 cases and was likewise confined to the premenopausal group. Overall, infectious lesions were more commonly encountered among premenopausal women, paralleling the higher frequency of inflammatory cervical smears observed in this group.

DISCUSSION

Cervical cancer continues to represent a major public health concern worldwide, particularly in low- and middle-income countries where organized screening programs remain suboptimal despite advances in preventive strategies and HPV vaccination. Early detection of premalignant cervical lesions through cytological screening remains an effective approach for reducing cervical cancer-related morbidity and mortality [8, 9]. The present study evaluated the spectrum of cervical cytological findings in premenopausal and postmenopausal women using Liquid-Based Cytology (LBC) and demonstrated significant differences in cytomorphological patterns according to menopausal status. The overall smear adequacy rate in the present study was 98.3%, with only 1.7% of smears being unsatisfactory. This high adequacy rate may be attributed to the use of LBC, which provides improved cellular preservation, cleaner background, reduced obscuring blood and inflammatory exudate, and more uniform cell distribution compared with conventional smear techniques [5], [11]. Similar studies have reported superior specimen adequacy and improved diagnostic yield with LBC-based cervical screening [5], [11]. The high adequacy observed in the present study supports the continued utility of LBC as an effective cervical cancer screening modality in routine clinical practice.

Inflammatory smears constituted the most common cytological finding, accounting for 45.1% of all satisfactory smears and occurring significantly more frequently among premenopausal women than postmenopausal women (54.7% vs. 31.6%). Similar

observations have been reported in previous Indian studies where inflammatory lesions represented the predominant cytological abnormality detected during cervical screening [10, 11]. The higher prevalence of inflammatory smears among premenopausal women may be explained by active reproductive physiology, hormonal influences, and alterations in vaginal microbiota, and increased susceptibility to infectious and inflammatory conditions during the reproductive years. Recognition of inflammatory changes remains important because marked inflammation may occasionally obscure epithelial abnormalities and complicate cytological interpretation.

A major finding of the present study was the strong association between postmenopausal status and atrophic cervical changes. Atrophic smears were identified in 24.2% of postmenopausal women compared with only 3.6% of premenopausal women, while atrophic smears with inflammation accounted for 11.9% and 0.7% of cases, respectively. Statistical analysis demonstrated significantly increased odds of atrophic smears among postmenopausal women (OR=8.44; 95% CI: 4.81–14.81) and an even stronger association for atrophic inflammatory smears (OR=19.70; 95% CI: 6.01–64.51). These findings are consistent with previous studies that identified atrophic changes as a characteristic cytological feature of the postmenopausal cervix [6], [14].

The increased prevalence of atrophic smears among postmenopausal women is attributable to estrogen deficiency, which leads to thinning of the squamous epithelium, depletion of glycogen, epithelial fragility, and predominance of parabasal cells. These cytological alterations may produce nuclear hyperchromatic, increased nuclear-to-cytoplasmic ratio, and degenerative cellular changes that can mimic squamous intraepithelial lesions [6], [14]. Consequently, awareness of menopausal cytomorphological changes is essential to avoid over interpretation and reduce false-positive diagnoses in routine cytopathology practice.

Negative for intraepithelial lesion or malignancy (NILM) was reported in one-third of the study population and was less frequent among postmenopausal women than premenopausal women. This observation likely reflects the increased prevalence of age-related atrophic and inflammatory changes in the postmenopausal cervix, which contribute substantially to the cytological spectrum observed in this age group. The lower odds of NILM findings among postmenopausal women further emphasize the influence of hormonal status on cervical epithelial morphology.

Epithelial cell abnormalities were uncommon in the present study and accounted for only 0.7% of satisfactory smears. Two cases of ASC-US were identified among postmenopausal women, while isolated cases of LSIL, HSIL, and squamous cell carcinoma were observed in the premenopausal group. Although the prevalence of epithelial abnormalities was low, their detection remains clinically significant because squamous intraepithelial lesions represent

recognized precursor lesions in cervical carcinogenesis. Similar low frequencies of epithelial abnormalities have been reported in population-based cervical cytology studies conducted in India [10–12]. The low prevalence observed in the present study may reflect the screening nature of the study population and the relatively small proportion of women presenting with clinically significant cervical pathology.

Among infectious lesions, candidiasis demonstrated a comparable distribution between premenopausal and postmenopausal women, whereas *Trichomonas vaginalis* infection and bacterial vaginosis were observed exclusively among premenopausal women. The predominance of infectious lesions in premenopausal women may be related to hormonal influences, reproductive activity, and alterations in the vaginal microenvironment. Infectious and inflammatory conditions remain important considerations in cervical cytology because reactive epithelial atypia associated with infection may occasionally mimic epithelial abnormalities and contribute to diagnostic uncertainty [18].

The findings of the present study reinforce the continued importance of cervical cytology screening, particularly in resource-constrained settings where HPV-based screening may not be universally available. Although contemporary screening guidelines increasingly emphasize HPV testing and co-testing strategies, cytology continues to provide a practical, accessible, and cost-effective method for cervical cancer screening in many developing regions [15, 16]. Recognition of age-related cytomorphological variations, especially the predominance of inflammatory lesions among premenopausal women and atrophic changes among postmenopausal women, is essential for accurate interpretation of cervical smears and avoidance of diagnostic pitfalls.

The present study has certain limitations. Its retrospective design and single-center setting may limit generalizability of the findings. Histopathological correlation and HPV testing were not available for all cases, precluding detailed evaluation of the relationship between cytological findings and underlying cervical pathology. Furthermore, the relatively low number of epithelial abnormalities limited subgroup analysis of premalignant and malignant lesions. Future multicentre studies incorporating HPV testing, histopathological follow-up and larger populations may provide further insight into the influence of menopausal status on cervical cytomorphological and cervical cancer risk.

Overall, the present study demonstrates distinct menopausal variations in cervical cytological findings, with inflammatory lesions predominating among premenopausal women and atrophic alterations showing a strong association with postmenopausal status. These findings highlight the importance of considering menopausal status during cytological interpretation and support the continued role of LBC-based cervical screening in routine clinical practice.

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