Research Article

Spectrum of PAP Smear Cytology According to the Bethesda System 2014 in Perimenopausal Women Presenting in a Tertiary Care Centre in North India

Surbhi Mahajan[*]

Background: Perimenopausal women, owing to fluctuating hormonal status, are prone to bleeding disorders and cervical epithelial changes, making Papanicolaou smear screening clinically important in this age group. This study aimed to evaluate the demographic profile, presenting complaints, specimen adequacy, and spectrum of cervical cytological findings, using the Bethesda System 2014, in perimenopausal women over a two-year period.

Methods: This retrospective-prospective observational study was conducted in the Department of Pathology, Government Medical College, Kathua, from January 2024 to December 2025. A total of 490 perimenopausal women aged 40–55 years who underwent cervical screening were included. Cytological findings were categorized according to the Bethesda System 2014, and specimen adequacy was assessed.

Results: A total of 960 cervical Pap smear samples were examined, of which 490 (51.0%) were from perimenopausal women and constituted the study population, the majority belonged to the 40–44 years age group (60.0%). Abnormal uterine bleeding was the most common presenting complaint (62.0%). Of the cervical cytology samples, 445 (90.8%) were satisfactory for evaluation. Negative for intraepithelial lesion or malignancy (NILM) was observed in 418 (93.9%) cases, with inflammatory changes constituting the predominant finding. Epithelial cell abnormalities were identified in 27 (6.1%) cases, including ASC-US in 11 (2.5%), LSIL in 6 (1.3%), HSIL in 4 (0.9%), squamous cell carcinoma in 3 (0.7%), ASC-H in 2 (0.4%), and AGC in 1 (0.2%) case.

Conclusions: Cervical cytology remains a valuable screening tool in perimenopausal women, detecting a clinically significant burden of epithelial abnormalities alongside predominantly reactive findings, and supports continued screening throughout this transition irrespective of age or symptom severity.

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Introduction

Cervical cancer remains one of the most significant gynecological malignancies worldwide. According to GLOBOCAN 2024 estimates, it continues to be a major cause of cancer-related morbidity and mortality among women.[1] Despite being largely preventable through organized screening and early detection, cervical cancer remains a substantial public health challenge in India, reflecting persistent gaps in awareness, screening uptake, and follow-up care.[2,3]

Persistent infection with high-risk human papillomavirus (HPV) is recognized as the principal etiological factor in cervical carcinogenesis, and progression from HPV infection to invasive cancer generally occurs over several years through identifiable precursor lesions, providing an important opportunity for early detection and intervention.[4,5]

The Papanicolaou (Pap) smear remains one of the most successful screening tools because of its simplicity, affordability, and proven ability to detect premalignant and malignant cervical lesions at an early and treatable stage.[6,7] In addition to identifying epithelial abnormalities, cervical cytology provides useful information regarding inflammatory, infectious, and reactive changes affecting the cervix and vagina.[8] To standardize reporting and facilitate communication between cytopathologists and

Affiliations

Correspondence to: Surbhi Mahajan, affiliation. E-mail: surbzmjh.19@gmail.com

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clinicians, the Bethesda System was developed and subsequently revised, with the Bethesda 2014 update remaining the current internationally accepted reporting framework.[9,10]

Perimenopause, the transitional phase preceding and immediately following the final menstrual period, usually occurring between 40 and 55 years of age, represents a biologically distinct stage in a woman's reproductive life characterized by fluctuating hormone levels, menstrual irregularity, and progressive atrophic changes in the genital tract epithelium.[11] Hormonal alterations during this period may influence epithelial maturation and produce cytological patterns such as parabasal cell predominance, reactive nuclear atypia, inflammatory changes, and epithelial atrophy that may mimic or obscure true epithelial abnormalities, thereby posing diagnostic challenges in cervical cytology interpretation.[12,13]

Methodology:

Study design and setting

This ambispective observational study was conducted in the Department of Pathology, Government Medical College (GMC), Kathua, over a two-year period (1 January 2024 to 31 December 2025).

Study population

Perimenopausal women aged 40 to 55 years, classified per the STRAW+10 criteria,[7] who underwent Pap smear examination during the study period were included. Women with a prior hysterectomy, known cervical malignancy, or pregnancy were excluded.

Table 1: Demographic Profile of Study Population (n = 490)

Parameter	*Category*	*n*	*%*
Age group (years)	40–44	294	60.00
	45–49	140	28.57
	50–55	56	11.43
Parity	Nulliparous	7	1.43
	Parous	483	98.57
Presenting complaint	Abnormal uterine bleeding	304	62.04
	Post-menopausal bleeding	7	1.43
	Discharge per vaginum	47	9.59
	Routine screening	56	11.43
	Post-coital bleeding	12	2.45
	Pain abdomen	64	13.06

Table 2: Specimen Adequacy

Adequacy	*n*	*%*
Satisfactory for evaluation	445	90.82
Unsatisfactory	45	9.18
Total	490	100.00

Table 3: Overall Spectrum of Cytological Diagnoses (Bethesda 2014) — Satisfactory Smears (n = 445)

Bethesda Category	*n*	*%*
NILM	418	93.93
– Inflammatory/ Atrophic changes	404	90.79
– Trichomonas vaginalis	1	0.22
– Candida spp.	2	0.45
– Bacterial vaginosis pattern	11	2.47
Epithelial abnormalities (subtotal)	27	6.07
ASC-US	11	2.47
ASC-H	2	0.45
LSIL	6	1.35
HSIL	4	0.90
Squamous cell carcinoma	3	0.67
AGC (NOS/favor neoplastic)	1	0.22
AIS	0	0.00
Adenocarcinoma	0	0.00
Total	445	100.00

Sample collection and processing

Cervical samples were collected as liquid-based cytology preparations in the BD SurePath collection vial, employing broom-device collection into ethanol-based preservative fluid, followed by processing and modified Papanicolaou staining. Smears were reported by cytopathologists according to The Bethesda System for Reporting Cervical Cytology (2014), encompassing specimen adequacy, negative for intraepithelial lesion or malignancy (NILM, with organism- and inflammation-related subcategories), and squamous or glandular epithelial cell abnormalities (ASC-US, ASC-H, LSIL, HSIL, squamous cell carcinoma, AGC, AIS, and adenocarcinoma).

Data collection and analysis

Relevant demographic and clinical details were obtained from laboratory records and patient requisition forms. Data were analyzed using descriptive statistical methods. Categorical variables were expressed as frequencies and

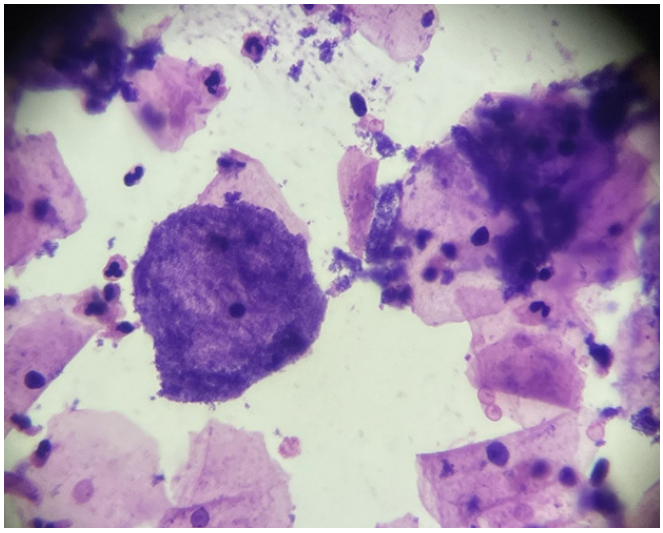

Figure 1: Smear showing clue cell in a case of bacterial vaginosis (PAP, 40x)

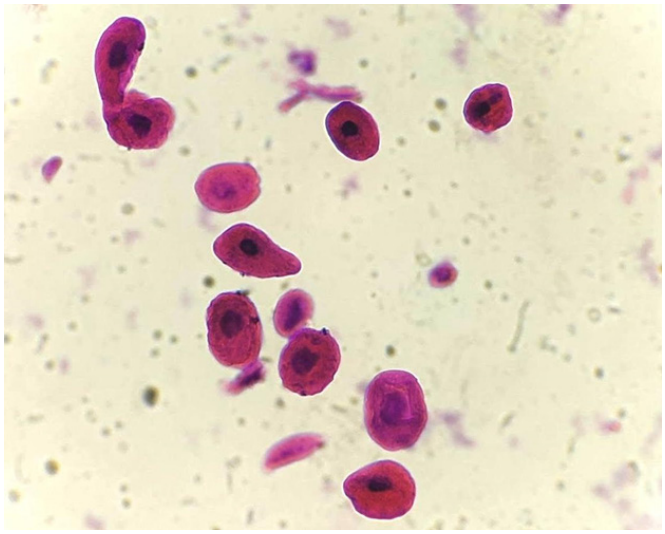

Figure 2: Numerous parabasal cell in case of Atrophic smear (Pap, 40x)

percentages. The distribution of cytological findings was assessed according to age groups, parity, presenting complaints, and specimen adequacy. Percentages were calculated for the respective categories and summarized in tables.

Ethical Considerations

The study was conducted after obtaining approval from the Institutional Ethics Committee of Government Medical College (GMC), Kathua. Ethical clearance was obtained prior to commencement of the study (Approval No. IEC/GMCK/52 dated 29-05-2024).

Results

A total of 960 cervical cytology samples were examined over the two-year study period, of which 490 (51.0%) were from perimenopausal women (40–55 years) and formed the study population.

Demographic and Clinical Profile

The majority of women were in the 40–44-year age group (294, 60.0%), followed by 45–49 years (140, 28.6%) and 50–55 years (56, 11.4%). Most women were parous (483, 98.6%), with only 7 (1.4%) being nulliparous. Abnormal uterine bleeding was the most common presenting complaint (304, 62.0%), followed by pain abdomen (64, 13.1%), routine screening (56, 11.4%), discharge per vaginum (47, 9.6%), post-coital bleeding (12, 2.4%), and post-menopausal bleeding (7, 1.4%). (Table 1).

Specimen Adequacy

Of the 490 smears, 445 (90.8%) were satisfactory for evaluation, while 45 (9.2%) were deemed unsatisfactory due to reasons such as scant cellularity, obscuring blood or inflammation, and air-drying artifact (Table 2)..

Cytological Spectrum According to Bethesda System 2014

Among the 445 satisfactory smears, 418 (93.9%) were reported as Negative for Intraepithelial Lesion or Malignancy (NILM). Inflammatory changes constituted the largest subgroup within NILM, accounting for 404

Table 4: Distribution of Epithelial Cell Abnormalities Across Perimenopausal Age Subgroups

Category	*40–44 yrs(n=294)*	*45–49 yrs(n=140)*	*50–55 yrs(n=56)*	*Total (n)*
ASC-US	2 (0.68%)	2 (1.43%)	7 (12.50%)	11
ASC-H	1 (0.34%)	1 (0.71%)	0 (0.00%)	2
LSIL	4 (1.36%)	1 (0.71%)	1 (1.79%)	6
HSIL	1 (0.34%)	2 (1.43%)	1 (1.79%)	4
SCC	1 (0.34%)	1 (0.71%)	1 (1.79%)	3
Glandular abnormalities	0 (0.00%)	1 (0.71%)	0 (0.00%)	1

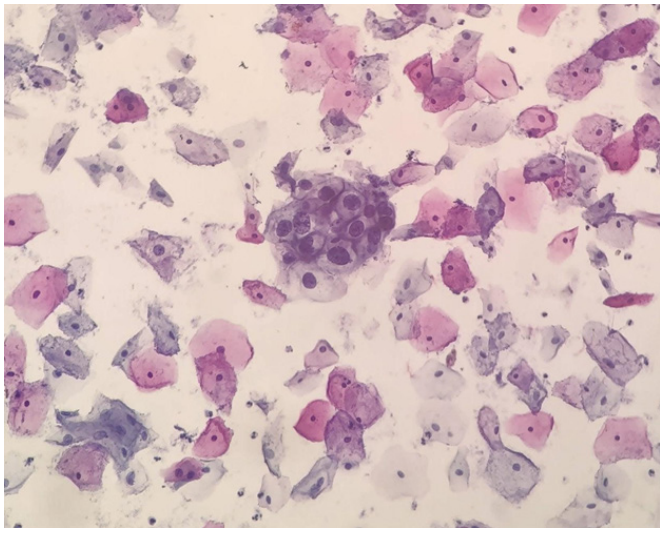

Figure 3: Low grade Squamous intraepithelial lesion (Pap, 10x)

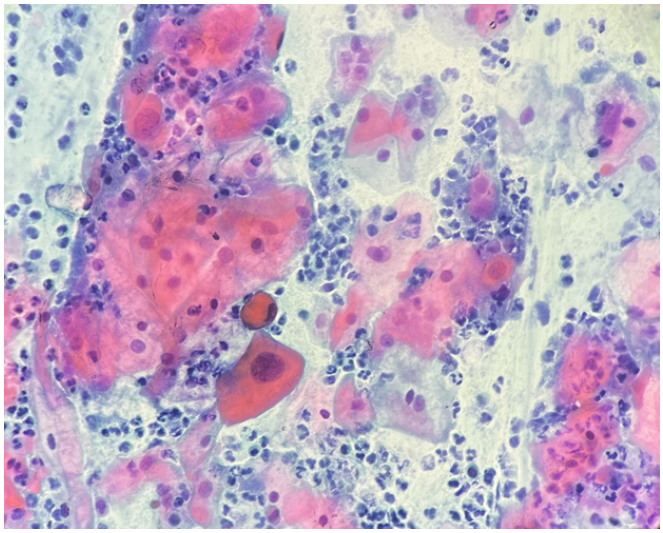

Figure 4: Atypical squamous cell of Undetermined Significance ASC-US (PAP, 40x)

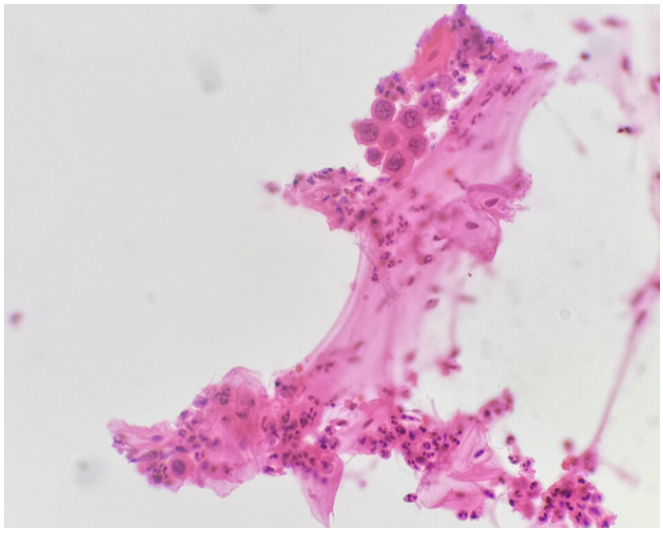

Figure 5: High grade Squamous intraepithelial lesion (PAP, 10x)

(90.8%) cases. Infectious organisms identified included bacterial vaginosis pattern in 11 (2.5%) cases, Candida species in 2 (0.4%) cases, and Trichomonas vaginalis in 1 (0.2%) case.

Epithelial cell abnormalities were identified in 27 (6.1%) cases. Atypical squamous cells of undetermined significance (ASC-US) were the most frequent epithelial abnormality, observed in 11 (2.5%) cases, followed by low-grade squamous intraepithelial lesion (LSIL) in 6 (1.3%) cases, high-grade squamous intraepithelial lesion (HSIL) in 4 (0.9%) cases, squamous cell carcinoma (SCC) in 3 (0.7%) cases, atypical squamous cells-cannot exclude HSIL (ASC-H) in 2 (0.4%) cases, and atypical glandular cells (AGC) in 1 (0.2%) case. No cases of adenocarcinoma in situ (AIS) or adenocarcinoma were encountered (Table 3).

Age-wise Distribution of Epithelial Cell Abnormalities

Analysis of epithelial abnormalities across different perimenopausal age groups revealed that ASC-US was most frequently observed in women aged 50–55 years (7 cases), whereas LSIL was predominantly seen in the 40–44 years age group (4 cases). HSIL was more common among women aged 45–49 years (2 cases). Cases of squamous cell carcinoma were distributed equally across all age groups, with one case each in the 40–44, 45–49, and 50–55 years categories. A single case of atypical glandular cells was observed in the 45–49 years age group (Table 4).

Discussion

The present study evaluated the cytomorphological spectrum of cervical lesions in perimenopausal women using liquid-based cytology (LBC) and Bethesda System 2014 reporting criteria in a tertiary care hospital of North India.

Among the 960 cervical cytology samples received during the study period, 490 (51.0%) belonged to perimenopausal women, constituting slightly more than half of all cervical smears received over the two-year study period. This finding reflects the substantial contribution of women in the menopausal transition period to routine cervical screening services. The majority of patients were in the 40 to 44-year age group (60.0%), consistent with the early menopausal transition described by Harlow *et al*.[11] and Long *et al*.[13]

Abnormal uterine bleeding emerged as the most common indication for cervical smear examination, accounting for 62.0% of cases. This observation is consistent with the hormonal fluctuations and menstrual irregularities characteristic of the menopausal transition.

Tian *et al*.[14] similarly linked age-related hormonal and endometrial change to AUB in perimenopausal women.

The specimen adequacy rate in the present study was 90.8%, while only 9.2% of smears were unsatisfactory. This high adequacy rate supports the advantages of liquid-based cytology, which has been shown to improve specimen quality, reduce obscuring inflammatory and hemorrhagic material, and enhance the detection of epithelial abnormalities compared with conventional cytology.[8,9]

Negative for intraepithelial lesion or malignancy (NILM) was the predominant cytological category in the present study, accounting for 93.9% of satisfactory smears. This observation is consistent with contemporary cervical screening literature, where the majority of screened women demonstrate benign cytological findings.[15,8] Infective organisms including *Trichomonas vaginalis*, *Candida* species, and bacterial vaginosis pattern (Figure 1) were identified in a small proportion of cases, highlighting the additional diagnostic utility of cervical cytology in detecting genital tract infections alongside its primary screening role.[8]

Epithelial cell abnormalities were identified in 6.1% of satisfactory smears. ASC-US (Figure 4) was the most common epithelial abnormality, accounting for 2.5% of cases. Similar observations have been emphasized in Bethesda-based reporting literature, where ASC-US remains the most frequently encountered epithelial abnormality in routine cervical cytology practice.[15,10] Li *et al*.[12] further demonstrated that atrophic epithelial changes associated with estrogen deficiency may contribute to increased ASC-US interpretations among peri- and postmenopausal women. These findings support the possibility that hormonal alterations during perimenopause influence cytological interpretation and may partly explain the predominance of ASC-US observed in the present study.

LSIL (Figure 3) and HSIL (Figure 5) accounted for 1.3% and 0.9% of cases, respectively. The identification of these precursor lesions reinforces the continued value of cervical cytology in detecting clinically significant abnormalities before progression to invasive disease.[16,6] The presence of HSIL in perimenopausal women highlights the importance of maintaining regular cervical screening throughout the menopausal transition despite declining reproductive activity.

Three cases (0.7%) of squamous cell carcinoma (Figure 6) were identified in the present study. Although the prevalence was low, the detection of invasive carcinoma through routine cytological screening underscores the continuing burden of cervical cancer, particularly in low- and middle-income countries.[1,3,17,18] The identification of invasive malignancy through opportunistic screening further emphasizes the importance of sustained screening efforts and timely follow-up of abnormal cytological findings.

Age-wise analysis revealed a greater frequency of epithelial abnormalities among women aged 50–55 years, particularly ASC-US. Similar findings were reported by Li *et al*.[12], who attributed the increased frequency of ASC-US in older women to estrogen-deficiency–related atrophic and reactive epithelial alterations. Such age-related cytomorphological changes may complicate interpretation and warrant careful evaluation in women approaching menopause.

HSIL and squamous cell carcinoma were distributed across all age groups without a clear age predilection, indicating that clinically significant cervical lesions may occur throughout the perimenopausal period and should not be excluded on the basis of age alone. Continued participation in cervical cancer screening programs therefore remains essential for early detection and prevention of cervical cancer in this population.[6,7]

No cases of adenocarcinoma in situ or invasive adenocarcinoma were encountered in the present study. Similar observations have been reported in several cervical cytology studies where glandular lesions are considerably less frequent than squamous epithelial abnormalities.[10]

Conclusion

Papanicolaou smear screening remains a valuable, low-cost tool for evaluating perimenopausal women, in whom abnormal uterine bleeding is the predominant presenting complaint. In this study, NILM was the most common finding, largely inflammatory/Atrophic, while epithelial cell abnormalities were seen in 6.1% of satisfactory smears, with ASC-US the most frequent abnormality and a small but significant proportion of HSIL and squamous cell carcinoma. Epithelial cell abnormalities did not show a statistically significant association with age, while high-grade lesions and carcinoma occurred across the perimenopausal age groups, supporting the importance of continued cervical screening throughout the menopausal transition.

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