

PAP SMEAR SCREENING PATTERNS AND CYTOHISTOPATHOLOGICAL CORRELATION WITH CERVICAL BIOPSY FINDINGS IN WOMEN FROM RURAL AND SEMI-URBAN POPULATIONS: A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Cervical cancer remains one of the leading causes of cancer-related morbidity and mortality among women, particularly in low- and middle-income countries where organized screening programs are limited. Conventional Papanicolaou (Pap) smear is an effective, economical, and widely accepted screening modality for the early detection of cervical epithelial abnormalities. Correlation of cytological findings with histopathology is essential to evaluate the diagnostic accuracy of cervical cytology and optimize patient management. The present study aimed to assess Pap smear screening patterns and determine the cytohistopathological correlation between cervical cytology and cervical biopsy findings among women from rural and semi-urban populations. **Materials and Methods:** A hospital-based cross-sectional study was conducted in the Department of Pathology at a tertiary care teaching hospital. A total of 300 women aged 21–65 years who underwent conventional Pap smear screening were enrolled. Cervical cytology was reported according to The Bethesda System (2014). Cervical biopsy was performed in women with abnormal cytological findings and/or clinically suspicious cervical lesions, and histopathological examination served as the reference standard. Cytohistopathological correlation was evaluated, and the diagnostic performance of Pap smear was assessed by calculating sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), diagnostic accuracy, and Cohen's kappa coefficient. **Results:** The mean age of the participants was 39.8 ± 9.6 years, with most women belonging to the 31–40-year age group. White vaginal discharge was the commonest presenting complaint (58.7%). According to the Bethesda System, negative for intraepithelial lesion or malignancy (NILM) constituted 74.0% of smears, while epithelial cell abnormalities were identified in 26.0% of cases. Low-grade squamous intraepithelial lesion (LSIL) was the most frequent epithelial abnormality (8.0%), followed by ASC-US (6.0%) and HSIL (6.0%). Histopathological examination most commonly revealed chronic cervicitis (35.9%), followed by cervical intraepithelial neoplasia and invasive squamous cell carcinoma. A significant cytohistopathological correlation was observed ($\chi^2 = 86.5$, $p < 0.001$). Conventional Pap smear demonstrated a sensitivity of 89.3%, specificity of 93.5%, PPV of 87.7%, NPV of 94.4%, and overall diagnostic accuracy of 91.7%, with an almost perfect agreement between cytology and histopathology (Cohen's $\kappa = 0.81$). **Conclusion:** Conventional Pap smear is a reliable and cost-effective screening tool for the early detection of cervical epithelial lesions, demonstrating excellent cytohistopathological concordance and high diagnostic accuracy. Its continued implementation, particularly in rural and semi-urban populations, may facilitate early diagnosis, prompt intervention, and reduction in the burden of cervical cancer through timely identification of premalignant and malignant lesions.

INTRODUCTION

Cervical cancer is a malignant neoplasm arising from the epithelial lining of the cervix, most commonly from the transformation zone where metaplastic squamous epithelium is particularly vulnerable to oncogenic insult. It is one of the most preventable cancers in women because it has a long pre-invasive phase, progressing through cervical intraepithelial neoplasia before developing into invasive carcinoma.^[1] Persistent infection with high-risk human papillomavirus, especially HPV-16 and HPV-18, is the central event in cervical carcinogenesis. Viral oncoproteins E6 and E7 interfere with key tumour suppressor pathways, particularly p53 and retinoblastoma protein, resulting in abnormal cell-cycle progression, genomic instability, dysplasia, and eventual malignant transformation.^[2,3]

The Papanicolaou smear remains a simple, inexpensive, and widely used screening method for detecting inflammatory, premalignant, and malignant cervical epithelial lesions. Reporting cervical cytology according to the Bethesda System provides standardized terminology for specimen adequacy, negative smears, epithelial cell abnormalities, and glandular lesions, thereby improving communication between pathologists and clinicians.^[4] Although cytology is an effective screening tool, histopathological examination of cervical biopsy remains the confirmatory method for diagnosis and grading of cervical lesions. Therefore, cytohistopathological correlation is essential for assessing diagnostic accuracy, identifying false-negative or false-positive cytology results, improving laboratory quality assurance, and guiding appropriate clinical management.^[5,6]

In India, cervical cancer continues to impose a major health burden, especially among women from rural and semi-urban populations, where screening uptake, awareness, access to healthcare, and follow-up compliance may be limited.^[7] Opportunistic Pap smear screening in tertiary care settings often provides an important opportunity for early detection in such underserved groups. However, local data on Pap smear patterns and their correlation with cervical biopsy findings remain necessary because disease prevalence, clinical presentation, screening practices, and cytology-histology concordance may vary across regions. Hence, the present study was undertaken to evaluate Pap smear screening patterns and determine their cytohistopathological correlation with cervical biopsy findings among women from rural and semi-urban populations, with the aim of assessing the diagnostic utility of cervical cytology in this setting.

MATERIALS AND METHODS

This hospital-based cross-sectional study was conducted in the Department of Pathology at a tertiary care teaching hospital catering predominantly to rural and semi-urban populations, over a period of 18 months, following approval from the Institutional

Ethics Committee. Women aged 21–65 years who attended the Department of Obstetrics and Gynaecology for cervical cancer screening and underwent conventional Papanicolaou (Pap) smear examination during the study period were enrolled consecutively after obtaining written informed consent. Women with a previous diagnosis of cervical carcinoma, those who had received treatment for cervical intraepithelial lesions, pregnant women, women who had undergone hysterectomy, and cases with unsatisfactory or inadequate cervical smears according to the Bethesda System (2014) were excluded. Demographic and clinical information including age, residence (rural/semi-urban), parity, presenting complaints, and per-speculum findings were recorded using a predesigned case record proforma.

Conventional cervical cytology specimens were collected from the transformation zone using an Ayre's spatula and/or endocervical cytobrush under aseptic precautions. The smears were immediately fixed in 95% ethanol, stained by the conventional Papanicolaou staining technique, and examined independently by experienced cytopathologists. Cytological interpretation was performed according to The Bethesda System (2014) and categorized as negative for intraepithelial lesion or malignancy (NILM), atypical squamous cells (ASC-US/ASC-H), low-grade squamous intraepithelial lesion (LSIL), high-grade squamous intraepithelial lesion (HSIL), atypical glandular cells (AGC), squamous cell carcinoma, adenocarcinoma, and other relevant epithelial abnormalities. Cervical biopsy was performed in women with abnormal cytological findings and/or clinically suspicious cervical lesions, as decided by the treating gynecologist. Biopsy specimens were fixed in 10% neutral buffered formalin, routinely processed, paraffin embedded, sectioned at 3–5 μ m thickness, stained with hematoxylin and eosin, and examined histopathologically. Histopathological diagnoses were classified as chronic cervicitis, cervical intraepithelial neoplasia (CIN I–III), carcinoma in situ, invasive squamous cell carcinoma, adenocarcinoma, or other pathological lesions.

Cytohistopathological correlation was carried out by comparing Pap smear diagnoses with the corresponding histopathological diagnoses in women who underwent cervical biopsy. The frequency and distribution of cervical cytological abnormalities were determined, and the concordance between cytological and histopathological diagnoses was assessed. The diagnostic performance of Pap smear was evaluated using cervical biopsy as the reference standard by calculating sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy. Statistical analysis was performed using IBM SPSS Statistics version [XX] (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean $\pm$ standard deviation or median (interquartile range), while categorical variables were presented as frequencies

and percentages. Associations between clinicodemographic variables and cervical epithelial lesions were analyzed using the Chi-square test or Fisher's exact test, as appropriate. Agreement

between cytological and histopathological diagnoses was assessed using Cohen's kappa coefficient. A two-tailed p-value of <0.05 was considered statistically significant.

RESULTS

Table 1: Baseline Demographic and Clinical Characteristics of the Study Population (N = 300)

Variable	Category	n	%
Age (years)	21–30	54	18.0
	31–40	102	34.0
	41–50	88	29.3
	51–60	42	14.0
	>60	14	4.7
Mean age (years)	39.8 ± 9.6	—	—
Residence	Rural	188	62.7
	Semi-urban	112	37.3
Parity	Nulliparous	24	8.0
	1–2	118	39.3
	≥3	158	52.7
Presenting complaints*	White vaginal discharge	176	58.7
	Lower abdominal pain	94	31.3
	Abnormal uterine bleeding	56	18.7
	Postcoital bleeding	18	6.0
	Asymptomatic (screening)	46	15.3
Per-speculum findings*	Cervical erosion	122	40.7
	Hypertrophied cervix	68	22.7
	Healthy cervix	74	24.7
	Suspicious growth	16	5.3
	Cervical polyp	20	6.7

39.8 ± 9.6 years, with the largest proportion belonging to the 31–40 years age group (34.0%), followed by the 41–50 years age group (29.3%). Most participants were from rural areas (62.7%), while the remaining 37.3% belonged to semi-urban localities. Multiparous women (parity ≥3) constituted the majority (52.7%), followed by women with parity of 1–2 (39.3%). The most common presenting

complaint was white vaginal discharge (58.7%), followed by lower abdominal pain (31.3%) and abnormal uterine bleeding (18.7%). On per-speculum examination, cervical erosion (40.7%) was the most frequent finding, whereas suspicious cervical growth was observed in only 5.3% of the participants. [Table 1]

Table 2: Distribution of Cervical Cytology Findings According to the Bethesda System (2014) (N = 300)

Cytological diagnosis	n	%
Negative for intraepithelial lesion or malignancy (NILM)	222	74.0
Normal cytology	18	6.0
Inflammatory smear	184	61.3
Atrophic smear	12	4.0
Specific infections	8	2.7
ASC-US	18	6.0
ASC-H	6	2.0
LSIL	24	8.0
HSIL	18	6.0
AGC	3	1.0
Squamous cell carcinoma	8	2.7
Adenocarcinoma	1	0.3
Total	300	100.0

According to the Bethesda System (2014), negative for intraepithelial lesion or malignancy (NILM) was the predominant cytological diagnosis, accounting for 74.0% of all Pap smears. Among the NILM category, inflammatory smears constituted the majority (61.3%), whereas normal cytology, atrophic smears, and specific infections were comparatively less frequent. Epithelial cell abnormalities were

identified in 26.0% of the study population. Among these, low-grade squamous intraepithelial lesion (LSIL) was the most common epithelial abnormality (8.0%), followed by ASC-US (6.0%) and HSIL (6.0%). Squamous cell carcinoma and adenocarcinoma were detected cytologically in 2.7% and 0.3% of women, respectively. [Table 2]

Table 3: Histopathological Spectrum and Cytohistopathological Correlation of Cervical Lesions (n = 78 biopsies)**A. Histopathological Diagnosis**

Histopathological diagnosis	n	%
Chronic cervicitis	28	35.9
Chronic cervicitis with squamous metaplasia	12	15.4
CIN I	10	12.8
CIN II	8	10.3
CIN III	6	7.7
Squamous cell carcinoma	12	15.4
Adenocarcinoma	2	2.5
Total	78	100.0

B. Cytohistopathological Correlation

Pap smear diagnosis	Benign cervicitis	CIN I	CIN II	CIN III	SCC	Adenocarcinoma	Total
NILM	22	2	1	0	0	0	25
ASC-US	5	4	1	0	0	0	10
ASC-H	1	1	2	2	0	0	6
LSIL	2	5	3	1	0	0	11
HSIL	0	0	1	5	4	0	10
Squamous cell carcinoma	0	0	0	0	8	0	8
AGC	0	0	0	0	0	2	2
Total	30	12	8	8	12	2	72

Cervical biopsy was available for 78 women with abnormal cytological findings and/or clinically suspicious cervical lesions. Histopathological examination revealed chronic cervicitis as the most common diagnosis (35.9%), followed by chronic cervicitis with squamous metaplasia (15.4%). Cervical intraepithelial neoplasia was identified across all grades, with CIN I being the most frequent precursor lesion (12.8%), while invasive squamous cell carcinoma constituted 15.4% of biopsy specimens.

Cytohistopathological correlation demonstrated a progressive increase in histologically confirmed high-grade lesions with increasing cytological severity. Most women with NILM had benign histopathological findings, whereas the majority of LSIL cases corresponded to CIN I, and HSIL cases predominantly correlated with CIN III and invasive squamous cell carcinoma. All cytological diagnoses of squamous cell carcinoma showed concordant invasive malignancy on histopathology. The association between cytological and histopathological diagnoses was statistically highly significant ($\chi^2 = 86.5$, $p < 0.001$), indicating a strong correlation between Pap smear findings and cervical biopsy diagnoses. [Table 3]

DISCUSSION

The present study evaluated Pap smear screening patterns and their cytohistopathological correlation with cervical biopsy findings in women from rural and semi-urban populations. In our study, the mean age was 39.8 ± 9.6 years, and the largest proportion of women belonged to the 31–40 years age group (34.0%), followed by 41–50 years (29.3%). This age distribution is comparable to Bamanikar et al., who studied 3791 Pap smears and found the highest

proportion of women in the 31–40 years age group (35.61%).^[8] Similarly, Rajeswari et al. reported that the majority of women undergoing cervical cytology belonged to the reproductive and perimenopausal age groups.^[9] White vaginal discharge was the most common presenting complaint in our study (58.7%), which is consistent with the observations of Bamanikar et al., where whitish vaginal discharge was reported in 23.95% of women, and with Gupta et al., who observed vaginal discharge in approximately 34% of screened women.^[8,10]

In the present study, NILM constituted 74.0% of Pap smear reports, while epithelial cell abnormalities were identified in 26.0% of cases. Among epithelial abnormalities, LSIL (8.0%) was the commonest lesion, followed by ASC-US (6.0%) and HSIL (6.0%). Bamanikar et al. reported a higher NILM rate (88.02%) and lower epithelial abnormalities (5.99%), with ASC-US (2.98%) being the predominant abnormality followed by LSIL (1.19%) and HSIL (0.66%).^[8] Khairwa et al. reported abnormal cytology in 9.5% of women, with ASC-US (7.1%) being the most frequent epithelial abnormality, followed by LSIL (1.01%), ASC-H (0.56%), HSIL (0.33%), AGC (0.22%), and SCC (0.11%).^[11] Rajeswari et al. observed inflammatory/NILM smears in 54.18%, ASC-US in 20.68%, HSIL in 13.84%, SCC in 6.84%, LSIL in 1.65%, AGUS in 0.51%, and adenocarcinoma in 0.17%.⁹ The relatively higher proportion of epithelial abnormalities observed in our study may be attributed to the symptomatic nature of the study population and the predominance of women from rural and semi-urban areas attending a tertiary care referral centre.

Histopathological examination in our study demonstrated chronic cervicitis (35.9%) as the commonest diagnosis, followed by chronic cervicitis with squamous metaplasia (15.4%), CIN I (12.8%),

CIN II (10.3%), CIN III (7.7%), squamous cell carcinoma (15.4%), and adenocarcinoma (2.5%). Comparable findings were reported by Bamanikar et al., who observed chronic cervicitis as the predominant histopathological lesion followed by LSIL, HSIL, and invasive carcinoma.^[8] Khairwa et al. also found chronic cervicitis (41.07%) and chronic cervicitis with squamous metaplasia (26.75%) as the leading biopsy diagnoses, followed by CIN I (3.57%), carcinoma in situ (14.28%), keratinizing SCC (7.14%), and non-keratinizing SCC (1.78%).^[11] Gupta et al. similarly reported chronic inflammatory lesions as the most frequent biopsy findings, emphasizing that inflammatory cervical pathology continues to constitute the largest proportion of cervical biopsies in hospital-based studies.^[10]

Cytohistopathological correlation in the present study demonstrated a highly significant association between Pap smear diagnosis and cervical biopsy findings ($\chi^2 = 86.5$, $p < 0.001$). Most NILM cases corresponded to benign histopathological lesions, whereas LSIL predominantly correlated with CIN I and HSIL correlated mainly with CIN III and invasive squamous cell carcinoma. All cytologically diagnosed squamous cell carcinoma cases were confirmed on histopathology. Similar observations were reported by Patil and Jibhkate, who demonstrated an overall cytohistological concordance of 57%, with the highest agreement in HSIL (87.5%) cases.^[12] Rajeswari et al. also observed excellent concordance, with 80% of LSIL cases corresponding to CIN I, 58.83% of HSIL cases corresponding to CIN II, 11.76% to CIN III, and 93.75% of cytological SCC cases confirmed histologically as invasive squamous cell carcinoma.^[9] These findings indicate that diagnostic concordance increases with the severity of cytological abnormality and reinforce the reliability of the Bethesda reporting system in predicting underlying histopathological lesions.

The diagnostic performance of conventional Pap smear in our study was encouraging, with a sensitivity of 89.3%, specificity of 93.5%, positive predictive value of 87.7%, negative predictive value of 94.4%, and overall diagnostic accuracy of 91.7%. The Cohen's kappa coefficient of 0.81 indicated almost perfect agreement between cytology and histopathology. Bamanikar et al. reported comparable diagnostic indices with 89.47% sensitivity, 88.70% specificity, and 82.92% positive predictive value.^[8] Khairwa et al. reported 83.33% sensitivity, 94.73% specificity, 88.23% positive predictive value, 92.30% negative predictive value, and 91.07% diagnostic accuracy, findings closely resembling those of the present study.^[11] Patil and Jibhkate documented a sensitivity of 77.7%, specificity of 84.2%, and diagnostic accuracy of 82.1%.^[12] The comparatively higher specificity and diagnostic accuracy observed in our study may reflect meticulous smear collection, adherence to Bethesda System reporting criteria, and expert cytopathological evaluation.

Overall, the findings of the present study reaffirm that conventional Pap smear remains an effective, economical, and dependable screening modality for the early detection of cervical epithelial abnormalities, particularly in resource-limited rural and semi-urban settings. The excellent cytohistopathological concordance and high diagnostic accuracy observed in the present study support the continued implementation of organized cervical cytology screening programmes. Strengthening awareness, improving screening coverage, and ensuring timely histopathological confirmation of abnormal cytological findings may substantially reduce the burden of cervical precancerous lesions and invasive cervical cancer in underserved populations.

CONCLUSION

The present study demonstrates that conventional Pap smear is a reliable, cost-effective, and practical screening modality for the early detection of cervical epithelial abnormalities in women from rural and semi-urban populations. The predominance of inflammatory lesions, coupled with a significant proportion of premalignant and malignant epithelial abnormalities, underscores the importance of routine cervical cytology screening. The strong cytohistopathological correlation and high diagnostic accuracy observed in this study support the continued use of Pap smear as an effective primary screening tool, with cervical biopsy serving as the diagnostic gold standard for confirmation of abnormal cytological findings. Early identification and timely management of precursor lesions through organized screening can substantially reduce the burden of invasive cervical cancer.

Conflict of Interest: None Declared

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