



## Spectrum of Epithelial Cell Abnormality (ECA) and Cyto-Histopathological Correlation: A Hospital Based Prospective Study

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### KEYWORDS

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### ABSTRACT:

**Objective:** To determine the spectrum of cervical cytology and its correlation with histopathological findings in a tertiary care centre.

**Methods:** This was a hospital based prospective study conducted in the Vinayaka Missions Medical College & Hospital, Karaikal, Puducherry, India (tertiary care centre) between June 2022, and May 2023.

**Results:** Of the 442 requests for cytological examination – 5.2% were found to be unsatisfactory for evaluation, 80.8% smears were negative for intraepithelial lesion and malignancy and 7.9% had an epithelial cell abnormality (ECA). The distribution of smears showing signs of inflammation and atrophic changes were 5.0% and 1.1% respectively. Of the ECA, 14.3% had atypical squamous cells cannot exclude high-grade squamous intraepithelial lesion (ASC-H), 8.6% had low-grade squamous intraepithelial lesion (LSIL), 14.3% had high grade squamous intraepithelial lesion (HSIL), 11.4% had invasive squamous cell carcinoma, 2.8% had adenocarcinoma, and 5.7% had atypical glandular cells of undetermined significance (AGUS). Cytology and histopathology showed high rates of concordance for malignant lesions and AGUS. The assessment of diagnostic accuracy demonstrated the strength of cytology in identifying invasive squamous cell carcinoma and adenocarcinoma with 100% sensitivity, specificity, PPV, and NPV. However, variations were observed in the accuracy of identifying HSIL, LSIL, and negative cytology (NILM).

**Conclusion:** The high diagnostic accuracy for malignancies reinforces the pivotal role of cytology in identifying clinically significant lesions. However, the variations observed in the accuracy of identifying pre-neoplastic lesions call for a nuanced approach, potentially incorporating adjunctive testing and tailored surveillance strategies.

### Introduction:

Cervical carcinoma stands as a significant global health challenge, ranking as the second most prevalent cancer among women worldwide.(1) It poses a substantial threat to life in numerous developing countries, with India being no exception.(2) A research by Bamanikar et al.

indicates that the annual global incidence of cervical cancer reaches approximately 510,000 new cases, resulting in around 288,000 deaths.(3) This type of cancer typically afflicts individuals in their middle years, predominantly affecting women aged 40 and above.(4) Early detection significantly increases the chances of a cure, and the implementation of Papanicolaou/Pap test



screenings has played a pivotal role in reducing cervical cancer rates.(5)

Several risk factors contribute to the development of cervical carcinoma, including early sexual activity, multiple sexual partners, low socioeconomic status, and infection with the human papillomavirus (HPV).(6) Notably, HPV, specifically types 16 and 18, along with herpes simplex type 2 and cytomegalovirus, are implicated in over 70% of all cervical cancers.(7) Employing cytology and histopathological correlation as a widely accepted method for internal quality assurance aids in dissecting factors leading to diagnostic discrepancies. The use of cytopathology emerges as a valuable tool in the early detection and diagnosis of cervical cancer.

Against this background, the aim of the present study was to determine the spectrum of cervical cytology and its correlation with histopathological findings in a tertiary care centre.

## Materials and Methods

This was a hospital based prospective study conducted in the Department of Pathology in collaboration with the Department of Obstetrics and Gynaecology, Vinayaka Missions Medical College & Hospital, Karaikal, Puducherry, India (tertiary care centre) between June 2022, and May 2023. The study was approved by the Institute Human Ethics Committee (IHEC), Vinayaka Missions Medical College & Hospital. After obtaining necessary approvals from the Dean, Medical Superintendent, and the Head of Medical records department (MRD), the electronic medical records and laboratory information system were accessed. We obtained the sociodemographic characteristics, clinical complaints and per vaginal examination findings from the patient requisition form of all the patients who underwent Pap smear. However, we excluded patients with a history of hysterectomy and antenatal women.

The study resorted to complete enumeration of all Pap smears reported during the study period. The Pap smears were reported using the 2014 Bethesda system for reporting cervical cytology.(8) The specimen was considered adequate if it was satisfactory for evaluation (describe presence/absence of endocervical/transformation zone components and any other quality indicators – partially obscuring blood,

inflammation, etc.).(9) The general categorization was – Negative for intraepithelial lesion or malignancy (NILM); and Epithelial cell abnormality with specification of cell type, squamous/glandular as appropriate. The squamous epithelial cell abnormalities included,

1. Atypical squamous cells (ASC) – of undetermined significance (ASC-US); cannot exclude/rule out HSIL atypical squamous cells (ASC-H)
2. LSIL (encompassing HPV/mild dysplasia/CIN 1)
3. HSIL (encompassing moderate and severe dysplasia/CIS/CIN 2 and CIN 3)
4. With features suspicious for invasion (if suspected)
5. Squamous cell carcinoma.

The glandular epithelial cell abnormalities included,

- a. Atypical – Endocervical cells (NOS or specify); Endometrial cells (NOS or specify); Glandular cells (NOS or specify)
- b. Atypical – Endocervical cells (Favor neoplastic); Glandular cells (Favor neoplastic)
- c. Endocervical Adenocarcinoma in situ
- d. Adenocarcinoma – Endocervical; Endometrial; Extrauterine; NOS

Abnormal cytology correlation was done with histopathological findings in cases where cervical biopsy or total hysterectomy specimens were available. We ensured that the ethical principles were followed, and confidentiality was maintained throughout the study.

The data collected was entered in Microsoft Excel, coded, recoded, and analysed using Statistical Package for Social Sciences (SPSS) v23. Descriptive analysis was presented using numbers and percentages for categorical variables; mean and standard deviation (SD) for continuous variables. Appropriate graphs were used. The interrater reliability (IRR) method – percent agreement was computed between cytology and histopathology. The tests of diagnostic accuracy – sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were computed for cytology in relation to histopathology.

## Results

We received a total of 442 requests for cytological examination between June 2022, and May 2023. Out of those, 23 smears (5.2%) were found to be unsatisfactory for evaluation, 357 (80.8%) smears were negative for



intraepithelial lesion and malignancy and 35 smears (7.9%) had an epithelial cell abnormality (ECA). The distribution of smears showing signs of inflammation and atrophic changes were 5.0% and 1.1% respectively. In the inflammation category, bacterial vaginosis (16 smears, 72.7%) was the commonest finding followed by *Trichomonas* (4 smears, 18.2%) and *Candida* (2 smears, 9.1%).

Of the 419 smears included in the study, 70 were from women aged 20 to 30 years, 147 were from women aged 31 to 40 years, 137 were from women aged 41 to 50 years, 46 were from women 51 to 60 years, and 19 were from women above 60 years of age. Pain abdomen was the most common complaint, followed by menstrual irregularities, white discharge, urinary disturbances, mass per vaginum and postmenopausal bleeding, in that order.

**Spectrum of epithelial cell abnormality (ECA):** In the present study, a total of 35 smears presented with epithelial cell abnormalities (7.9%). Out of those, five smears had atypical squamous cells cannot exclude high-grade squamous intraepithelial lesion (ASC-H, 14.3%), three smears had low-grade squamous intraepithelial lesion (LSIL, 8.6%), five smears had high grade squamous intraepithelial lesion (HSIL, 14.3%), four smears had invasive squamous cell carcinoma (11.4%), one had adenocarcinoma (2.8%), and two smears had atypical glandular cells of undetermined significance (AGUS, 5.7%).

**Cyto-histopathological correlation:** Of the 419 patients with available cytology reports (after excluding 23 smears found to be unsatisfactory for evaluation from total 442 smears), 78 had their histopathological diagnosis – 43 of 357 (12.0%) with negative for intraepithelial lesion and malignancy; and all 35 with epithelial cell abnormality (100%).

The results showed that 44.2% of the cytology reports for NILM showed normal results in histopathology, and 55.8% showed chronic cervicitis. The other results were – of the 15 cytology reports of atypical squamous cells of undetermined significance (ASC-US), 26.7% showed normal, 26.7% showed chronic cervicitis, 26.7% showed LSIL, and 20.0% showed HSIL in histopathological examination; of the five cytology reports of atypical squamous cells cannot exclude high-grade squamous

intraepithelial lesion (ASC-H), 20.0% showed chronic cervicitis, 20.0% showed LSIL, 40.0% showed HSIL, and the other 20.0% showed malignancy in histopathological examination; of the three cytology reports of low-grade squamous intraepithelial lesion (LSIL), normal, chronic cervicitis and HSIL was observed in 33.3% each through histopathological examination; and of the five cytology reports of high grade squamous intraepithelial lesion (HSIL), three showed HSIL and two showed malignancy in histopathology. It was also found that 100% of cytology reports for invasive squamous cell carcinoma and adenocarcinoma matched the histopathological reports for malignancy; and 100% of cytology reports for atypical glandular cells of undetermined significance (AGUS) matched chronic cervicitis in histopathological examination.

**Diagnostic accuracy of cytology in comparison with histopathological examination:** The sensitivity, specificity, PPV and NPV of cytology was 100% in comparison with histopathological examination for invasive squamous cell carcinoma and adenocarcinoma. However, for HSIL the sensitivity, specificity, PPV and NPV was 67.3%, 99.1%, 50.0%, and 98.3%; and for LSIL 93.7%, 94.0%, 76.2% and 98.4% respectively. Importantly, the results showed that the sensitivity, specificity, PPV, and NPV of NILM diagnosis by cytology was 82.9%, 96.6%, 98.4% and 72.0% respectively in comparison with histopathological examination.

## Discussion

The study, conducted at Vinayaka Missions Medical College & Hospital, aimed to evaluate the spectrum of cervical cytology and its correlation with histopathological findings. A total of 442 cytological examinations were performed, with a notable 5.2% (23 smears) being deemed unsatisfactory for evaluation. Unsatisfactory smears can hinder accurate diagnosis, emphasizing the importance of proper sampling techniques and patient cooperation in obtaining quality cytological specimens.(10) The study revealed that 7.9% of the examined smears exhibited epithelial cell abnormalities (ECA). This aligns with global trends showing a significant prevalence of cervical abnormalities, reinforcing the necessity for regular screening programs.(11, 12) Early detection of ECAs is



crucial for timely intervention and the prevention of cervical cancer.(13) In the inflammation category, the study reported bacterial vaginosis as the most common finding (72.7%), followed by *Trichomonas* (18.2%) and *Candida* (9.1%). These results emphasize the multifactorial nature of cervical abnormalities, with infections playing a substantial role. The high prevalence of bacterial vaginosis is consistent with findings in other populations.(14, 15) Atrophic changes were observed in 1.1% of the smears, indicating a relatively lower frequency. The low prevalence may be attributed to the study population or demographic characteristics. Further exploration into the factors influencing atrophic changes in cervical cytology could offer valuable insights.(16)

The age-wise distribution of the study population highlighted that the majority of smears were from women aged 31 to 40 years, emphasizing the relevance of targeted screening in this age group. These findings align with established guidelines recommending routine cervical screening for women starting at age 30 (US Preventive Services Task Force, 2018).(17, 18) Clinical complaints associated with the studied population included pain abdomen, menstrual irregularities, white discharge, urinary disturbances, mass per vaginum, and postmenopausal bleeding. Pain abdomen emerged as the most common complaint, underscoring the need for comprehensive gynaecological evaluations to address prevalent issues and facilitate early diagnosis.

The investigation into the spectrum of epithelial cell abnormalities (ECA) in the present study revealed a total prevalence of 7.9% among the examined smears. These findings underscore the clinical importance of cervical cytology as a screening tool for detecting early cellular alterations associated with cervical neoplasia. Among the identified abnormalities, 14.3% of the smears exhibited ASC-H. ASC-H is a category in cervical cytology associated with significant uncertainty and potential for high-grade lesions.(19) The prevalence of LSIL was 8.6%, while HSIL was identified in 14.3% of the abnormal smears. These classifications represent distinct levels of cellular dysplasia, with LSIL indicating mild to moderate abnormalities and HSIL signalling a higher risk for progression to invasive cancer.(20) The study reported invasive squamous cell carcinoma in 11.4% of abnormal smears and adenocarcinoma in 2.8%. These findings underscore the critical role of cervical cytology

in early detection, as invasive carcinoma represents a more advanced stage of neoplastic progression. The identification of adenocarcinoma further emphasizes the need for vigilance, as these cases may present unique challenges in diagnosis and management.(21) AGUS were identified in 5.7% of abnormal smears. AGUS is a category associated with potential glandular lesions that may involve the endocervix, endometrium, or even extrauterine sites.(22) The presence of AGUS underscores the complexity of cervical cytology interpretation and the need for comprehensive follow-up investigations to determine the underlying pathology. The study also highlights the need for clear and standardized reporting guidelines to enhance communication between pathologists and clinicians.

A total of 419 patients were included in the correlation analysis, revealing a comprehensive representation of the studied population. Of the 357 patients with a cytological diagnosis of NILM, 44.2% demonstrated normal results in histopathology, while 55.8% exhibited chronic cervicitis. This observation aligns with previous studies highlighting the common occurrence of chronic cervicitis in routine cervical cytology.(23) The findings emphasize the importance of recognizing and managing non-neoplastic cervical changes to avoid unnecessary interventions. For the 15 cases with a cytological diagnosis of ASC-US, histopathological examination revealed a diverse spectrum. While 26.7% showed normal histology and chronic cervicitis each, 26.7% progressed to LSIL, and 20.0% advanced to HSIL. This variability underscores the challenges associated with interpreting ASC-US and the necessity for careful follow-up and management.(24, 25) Among the cases diagnosed as ASC-H in cytology, 20.0% showed chronic cervicitis, 20.0% progressed to LSIL, and 40.0% advanced to HSIL, while the remaining 20.0% revealed malignancy on histopathological examination. The significant association between ASC-H and HSIL/malignancy in histopathology supports the clinical importance of recognizing and managing ASC-H as a high-risk category.(26) For the three cytological diagnoses of LSIL, histopathological examination revealed a distribution of 33.3% each for normal histology, chronic cervicitis, and HSIL. This variability in outcomes reinforces the dynamic nature of LSIL, which can regress, persist, or progress, emphasizing the need for close monitoring and intervention.(27) The high



rates of concordance for malignant lesions and AGUS highlight the reliability of cytological examination in identifying malignant lesions, emphasizing its pivotal role in guiding clinical management.(28)

The evaluation of cytology's diagnostic accuracy in comparison with histopathological examination is crucial for assessing the reliability of cervical cytology as a screening tool. In this study, the diagnostic accuracy was notably high for invasive squamous cell carcinoma and adenocarcinoma, with 100% sensitivity, specificity, PPV, and NPV. This outcome underscores the robustness of cytological examination in identifying malignant lesions. For HSIL, cytology demonstrated lower sensitivity but high specificity – indicates that while cytology is effective in correctly identifying a significant portion of HSIL cases, there is a proportion of false-negative results. This emphasizes the importance of complementary diagnostic approaches, particularly in cases with high clinical suspicion or discordant results. The observed PPV of 50.0% suggests that among cases classified as HSIL by cytology, only half are confirmed as such in histopathological examination. This highlights the need for careful consideration and follow-up in cases with HSIL cytology to prevent unnecessary interventions in false-positive instances.(29) For LSIL, cytology exhibited high sensitivity and specificity – indicates that cytology is effective in both detecting and excluding LSIL. The PPV of 76.2% suggests that a substantial majority of cases identified as LSIL by cytology are confirmed as such in histopathology. This reinforces the clinical relevance of LSIL cytology results and the importance of appropriate follow-up strategies. The diagnostic accuracy for NILM is crucial as it constitutes a significant portion of screening results. In this study, the sensitivity, specificity, PPV, and NPV for NILM were 82.9%, 96.6%, 98.4%, and 72.0% respectively. The high specificity and PPV suggest that NILM cytology results are reliable in excluding significant pathology.(30) However, the lower sensitivity and NPV indicate that a proportion of cases with negative cytology may still harbour abnormalities. This emphasizes the importance of continued surveillance and screening at appropriate intervals.

## Conclusion

The present study conducted at Vinayaka Missions Medical College & Hospital in Karaikal, Puducherry,

India, offers a comprehensive exploration of the spectrum of cervical cytology and its correlation with histopathological findings in a tertiary care setting. The study elucidated the prevalence and distribution of cytological abnormalities, revealing diverse findings ranging from NILM to various grades of squamous intraepithelial lesions and invasive carcinomas. Notably, the identification of atypical squamous cells, high-grade lesions, and invasive carcinomas underscored the critical role of cytology in early detection and intervention. The cyto-histopathological correlation unveiled nuanced relationships between cytological diagnoses and subsequent histopathological outcomes. This analysis provided essential insights into the concordance and discordance across different diagnostic categories, emphasizing the need for careful follow-up and management strategies tailored to specific abnormalities. The assessment of diagnostic accuracy demonstrated the strength of cytology in identifying invasive squamous cell carcinoma and adenocarcinoma with 100% sensitivity, specificity, PPV, and NPV. However, variations were observed in the accuracy of identifying HSIL, LSIL, and negative cytology (NILM). These findings underscore the complexities of interpreting certain cytological categories and highlight opportunities for refinement in screening protocols.

The results of this study have direct implications for clinical practice. The high diagnostic accuracy for malignancies reinforces the pivotal role of cytology in identifying clinically significant lesions. However, the variations observed in the accuracy of identifying pre-neoplastic lesions call for a nuanced approach, potentially incorporating adjunctive testing and tailored surveillance strategies.

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