

FROM SCREENING TO DIAGNOSIS: ANALYZING THE CONCORDANCE AND DISCORDANCE OF PAP SMEAR AND HISTOPATHOLOGICAL EXAMINATION IN MALIGNANT NEOPLASM OF CERVICAL LESIONS

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ABSTRACT

Objective: The purpose of this study is to assess the correlation and accuracy of Pap smears in the diagnosis of cervical lesions by comparing cytological findings with histopathological test results.

Introduction: Cervical cancer is an important issue in public health, especially in developing countries. Early detection by screening programs is extremely important to reduce morbidity and mortality. Pap smears are often used as the primary screening tool for cervical cancer. However, accuracy and correlation with histopathological examination (HPE) should require continuous evaluation to ensure effective diagnosis and treatment.¹⁻⁵

Materials and Methods: A prospective study was conducted, and data from patients with abnormal cervical cytology or clinically unhealthy cervix were analyzed. Pap smear samples were collected and evaluated using the Bethesda System for Reporting Cervical Cytology. Subsequently, cervical biopsies were performed on patients with abnormal Pap smear results. Histopathological examination (HPE) was conducted on biopsy samples to confirm the diagnosis.

Statistical Analysis:

The correlation between Pap smear results and histopathological diagnoses was assessed. Chi-square tests were used to determine the level of correlation. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the Pap smear were calculated with histopathological findings as the gold standard.

INTRODUCTION

Cervical cancer remains a significant public health challenge, particularly in developing countries where screening and early detection programs are not universally accessible. The Papanicolaou test, commonly known as the Pap smear, is a widely used screening tool for detecting precancerous and cancerous lesions of the cervix. Despite its widespread application, the accuracy and correlation between Pap smear findings and histopathological examination (HPE) results continue to be subjects of ongoing evaluation.¹

The Pap smear test involves collecting cells from the cervix and examining them under a microscope to detect abnormalities. While the test is effective in screening for cervical cancer, its sensitivity and specificity can vary, necessitating follow-up with colposcopy and biopsy for abnormal results². Colposcopy, which involves a detailed examination of the cervix using a magnifying instrument, helps to identify areas of abnormality that may require biopsy³. The biopsy samples are then subjected to histopathological examination, which provides a definitive diagnosis⁴.

Histopathological examination remains the gold standard for diagnosis of cervical lesions and provides a final confirmation of cytological findings⁵. Integrating Pap smear screening with histopathological confirmation can significantly enhance early detection and treatment efforts. However, discrepancies in diagnosing low-grade squamous intraepithelial lesions, abbreviated as LSIL and atypical squamous cells of undetermined significance abbreviated as, ASC-US necessitate further refinement in screening protocols and diagnostic criteria⁶. By evaluating the cytohistological correlation and diagnostic accuracy of Pap smears, healthcare providers can improve screening protocols and ensure timely and accurate diagnosis of cervical lesions. This comprehensive approach is essential for improving early detection and treatment of cervical cancer, and ultimately reduces disease-related morbidity and mortality⁷.

This study aims to assess the correlation between Pap smear results and histopathological diagnoses at a tertiary care center. By analyzing data from women with abnormal cervical cytology, this research seeks to evaluate the diagnostic accuracy of Pap smears and highlight the importance of integrating colposcopy and HPE for precise diagnosis and effective management of cervical lesions.

AIM AND OBJECTIVES

The aim of the study is to evaluate the correlation and accuracy of the Pap smear test in diagnosing cervical lesions, specifically comparing its findings with colposcopy and histopathology results in women presenting with unhealthy cervix. The objectives are to assess the diagnostic accuracy of the Pap smear, compare its cytological findings with histopathological results, and determine the correlation between Pap smear, colposcopy, and histopathology. Additionally, the study seeks to identify discrepancies between these diagnostic methods and evaluate their clinical implications.

MATERIAL AND METHODS

The study was conducted at Saveetha Medical College, Thandalam, Chennai, from March 2023 to June 2024, including a total of 106 cases. All these cases underwent PAP smear tests, and histopathological examinations were warranted due to abnormal findings. In this study, descriptive statistics were used to present general data. Nominal or ordinal variables were compared using the Chi-square test. Statistical analyses were performed using Windows SPSS, version 10.1 (SPSS Inc., Chicago, Illinois, USA). A p-value of <0.05 was considered statistically significant.

INCLUSION CRITERIA

All females attending the gynecology OPD having abnormal PAP smear findings and Histopathological examination has to be done due to abnormal findings.

EXCLUSION CRITERIA

Patients not requiring Histopathological examination.

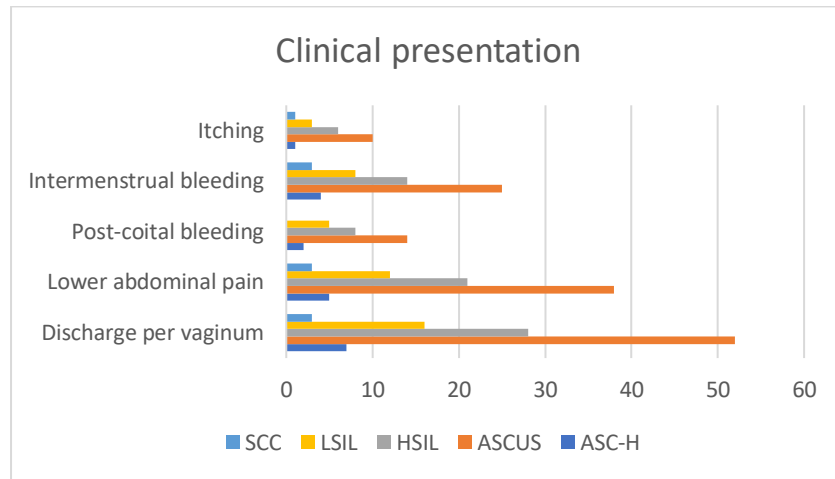
OBSERVATIONS AND RESULTS

A total of 106 patients were involved in this study. The clinical presentation of these patients is shown in the table below. The diagnosis is the diagnosis based on PAP smear findings.

Table 1: Clinical presentation

Diagnosis	Number of cases	Discharge per vaginum	Lower abdominal pain	Post-coital bleeding	Intermenstrual bleeding	Itching
ASC-H	7	7	5	2	4	1
ASCUS	52	52	38	14	25	10
HSIL	28	28	21	8	14	6
LSIL	16	16	12	5	8	3
SCC	3	3	3	3 (100%)*	3	1

Graph 1: Clinical Presentation



For patients diagnosed with ASC-H (Atypical Squamous Cells - cannot exclude HSIL), 7 experienced discharge per vaginum, 5 reported lower abdominal pain, 2 had post-coital bleeding, 4 had intermenstrual bleeding, and 1 experienced itching.

Among patients diagnosed with ASCUS (Atypical Squamous Cells of Undetermined Significance), 52 experienced discharge per vaginum, 38 reported lower abdominal pain, 14 had post-coital bleeding, 25 had intermenstrual bleeding, and 10 experienced itching. This group had the highest number of patients experiencing various symptoms.

For those diagnosed with HSIL (High-Grade Squamous Intraepithelial Lesion), 28 experienced discharge per vaginum, 21 reported lower abdominal pain, 8 had post-coital bleeding, 14 had intermenstrual bleeding, and 6 experienced itching.

Patients diagnosed with LSIL (Low-Grade Squamous Intraepithelial Lesion) reported 16 cases of discharge per vaginum, 12 of lower abdominal pain, 5 of post-coital bleeding, 8 of intermenstrual bleeding, and 3 of itching.

In the SCC (Squamous Cell Carcinoma) group, all 3 patients experienced discharge per vaginum, lower abdominal pain, post-coital bleeding (100%), intermenstrual bleeding, and 1 experienced itching. This indicates that post-coital bleeding is a prominent symptom among patients with SCC, highlighting its potential significance in the diagnosis of this severe condition. Overall, the table provides a clear overview of symptom distribution across different diagnoses, aiding in understanding the clinical presentation of cervical lesions.

PATHOLOGICAL FINDINGS

PAP smear findings	Histopathology Findings					Total
	Chronic cervicitis	Chronic with metaplasia	cervicitis squamous	LSIL	HSIL	SCC
ASCUS (n=52)	24	16		12	0	0
HSIL (n=28)	0	0		0	12	16
LSIL (n=16)	0	3		13	0	0
ASC-H (n=7)	0	0		3	2	2
SCC (n=3)	0	0		0	0	3
Total	24 (22.6%)	19 (17.9%)		28 (26.4%)	10 (9.4%)	21 (19.8%)
						106

This study aims to analyze the correlation between various PAP smear results and their corresponding histopathological findings, with a particular focus on the detection of Squamous Cell Carcinoma (SCC). The PAP smear categories examined include ASCUS (Atypical Squamous Cells of Undetermined Significance), HSIL (High-Grade Squamous Intraepithelial Lesion), LSIL (Low-Grade Squamous Intraepithelial Lesion), ASC-H (Atypical Squamous Cells - cannot exclude HSIL), and SCC. The histopathological diagnoses associated with these categories encompass Chronic Cervicitis, Chronic Cervicitis with Squamous metaplasia, LSIL, HSIL, and SCC. The primary objective was to evaluate the diagnostic accuracy of PAP smears for identifying SCC, focusing on key metrics such as sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

PAP Smear and Histopathological Findings

The study data indicates the distribution of histopathological diagnoses for each PAP smear result category:

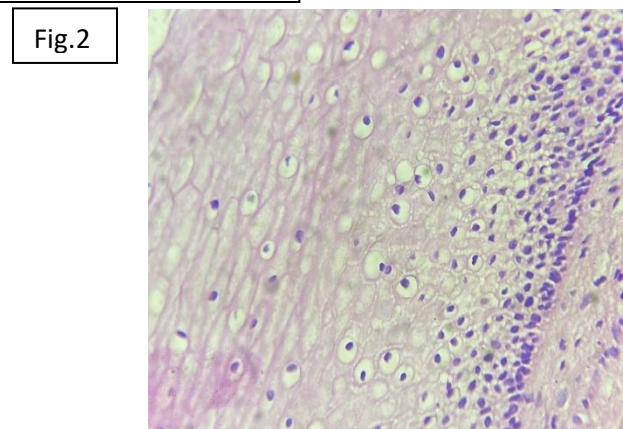
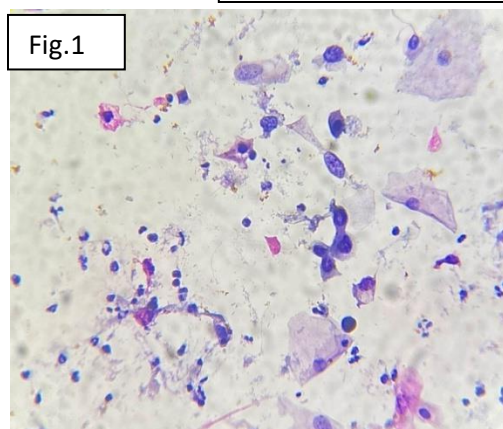
- **ASCUS:** Out of 52 cases, 24 were diagnosed with Chronic Cervicitis, 16 with Chronic Cervicitis with Squamous metaplasia, and 12 with LSIL.
- **HSIL:** Among 28 cases, 12 were confirmed as HSIL, and 16 were diagnosed as SCC.
- **LSIL:** From 16 cases, 3 were identified as Chronic Cervicitis with Dysplasia, and 13 were confirmed as LSIL.
- **ASC-H:** Out of 7 cases, 3 were diagnosed with LSIL, 2 with HSIL, and 2 with SCC.
- **SCC:** All 3 cases in this category were confirmed as SCC by histopathology.

Diagnostic Accuracy Metrics for SCC

The study's analysis of SCC detection using PAP smears revealed the following key metrics:

- **Sensitivity:** The ability of the PAP smear to correctly identify SCC cases (true positive rate) was 14.3%. This lower sensitivity indicates that some SCC cases were missed when they were present in non-SCC PAP smear categories. This reflects the occurrence of false negatives, where the PAP smear did not indicate SCC, but histopathology confirmed its presence.
- **Specificity:** The specificity of the SCC PAP smear was 100%, as no false positives were observed. All PAP smear results classified as SCC were confirmed as SCC by histopathology, demonstrating the PAP smear's ability to correctly identify patients without the disease.
- **Positive Predictive Value (PPV):** The PPV was 100%, showing that when a PAP smear result was positive for SCC, it reliably indicated the presence of SCC. This metric underscores the high confidence in positive SCC PAP smear results.
- **Negative Predictive Value (NPV):** The NPV was 81.8%, suggesting that when the PAP smear did not indicate SCC, it was usually accurate. This metric reflects the probability that subjects with a negative PAP smear result for SCC truly did not have the disease.

LSIL Correlation; Fig.1-Pap staining (40x), Fig.2-H&E (40x)



HSIL Correlation; Fig.3- Pap staining shows increased nuclear pleomorphism (insert- shows Multinucleation) (40x), Fig.4- Moderately differentiated SCC (H&E. 10x), (insert shows high power 40x).

Fig.3

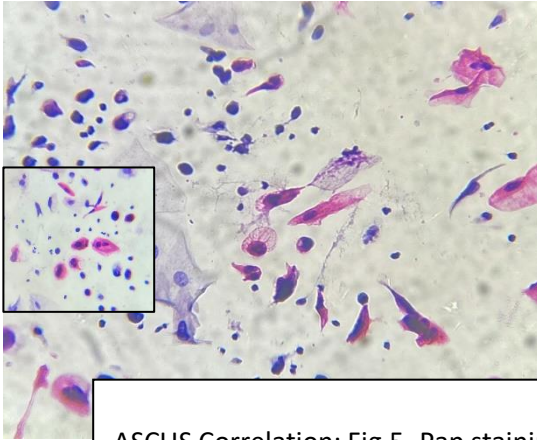
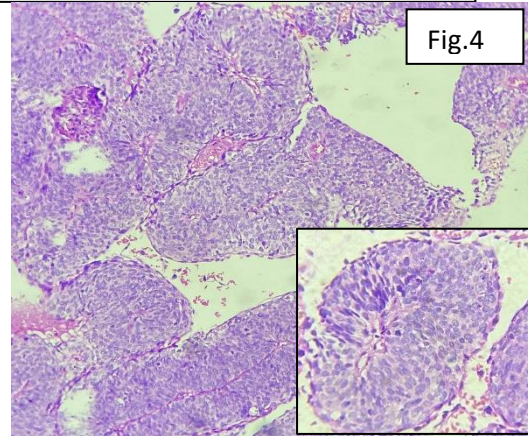


Fig.4



ASCUS Correlation; Fig.5- Pap staining shows increased nuclear pleomorphism (insert- Koilocytic changes) (40x), Fig.6-Chronic cervicitis with squamous metaplasia (H&E,40x). Fig.7- Chronic cervicitis (insert shows Lymphoplasmacytic inflammatory infiltrates. (H&E. 40x)

Fig.5

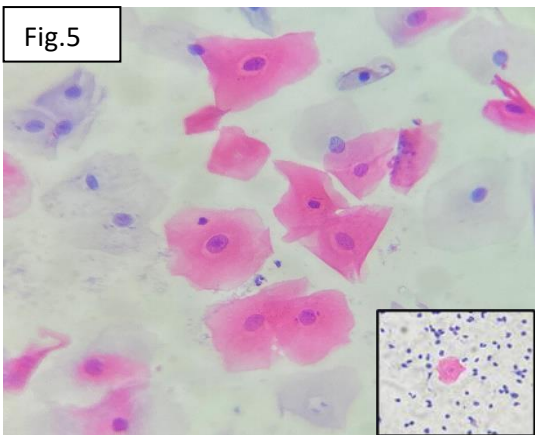
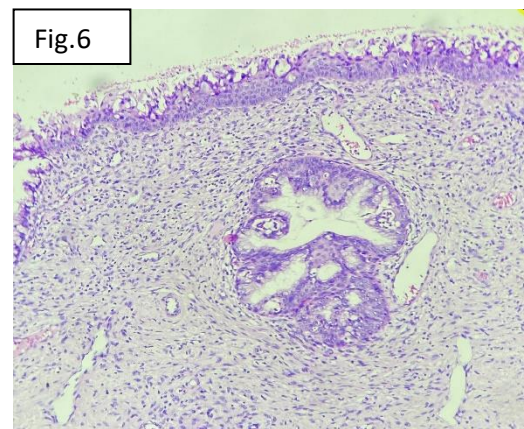
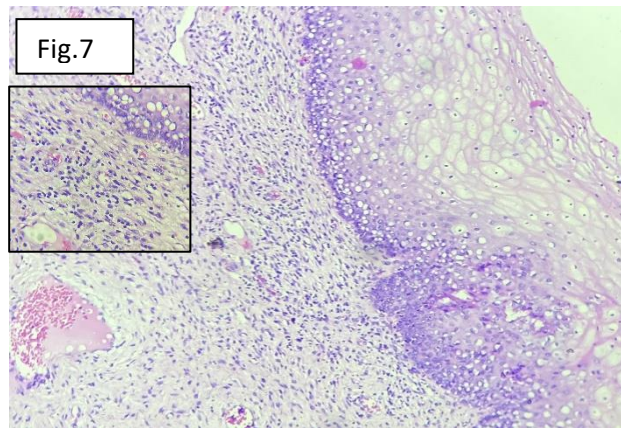
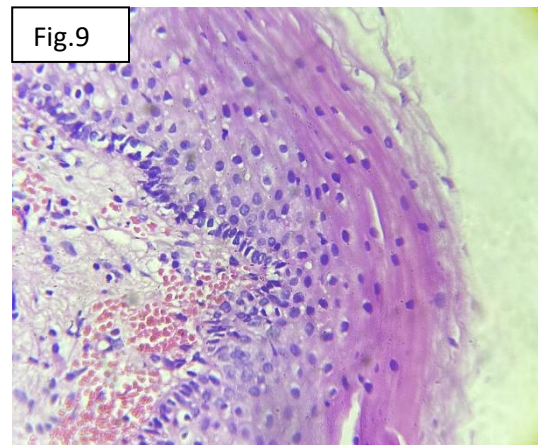
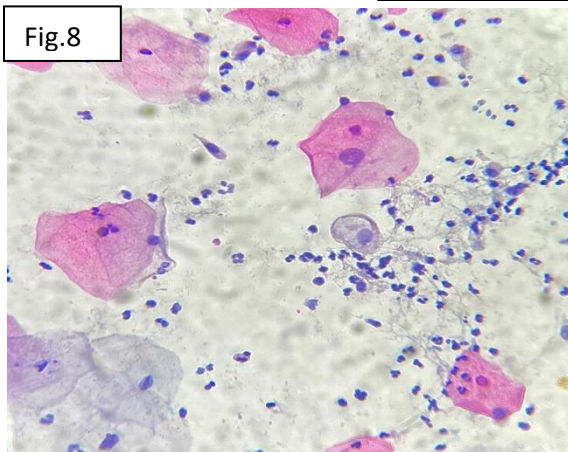


Fig.6

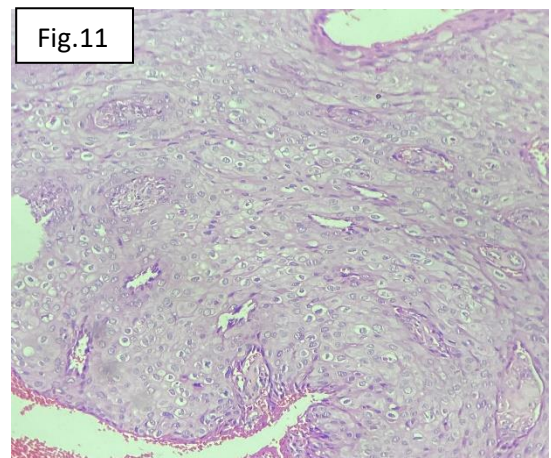
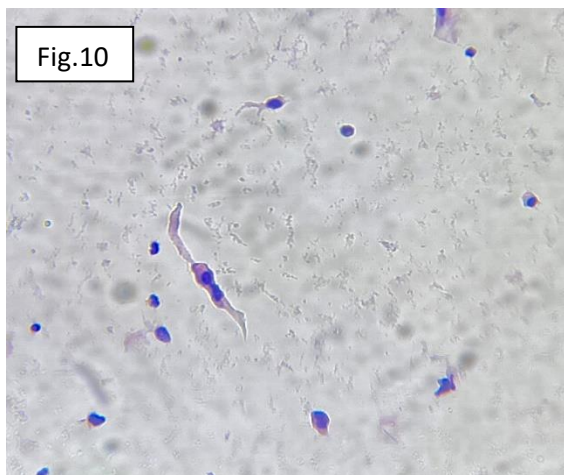




ASC-H- Fig.8- Pap Staining, 40x, Fig.9- HSIL (40x).



Squamous cell carcinoma(SCC) - Fig.10- Pap Staining shows Tadpole cell, 40x, Fig.11- Well differentiated SCC (H&E,10x).



STATISTICAL ANALYSIS

Key histopathological diagnoses considered are Chronic Cervicitis, Chronic Cervicitis with Squamous Metaplasia, HSIL, LSIL, Moderately Differentiated SCC, SCC, and Well-Differentiated SCC. The findings reveal distinct patterns, such as Chronic Cervicitis being most prevalent in ASCUS (46.2%) and LSIL (12.5%), while HSIL was predominantly detected in HSIL PAP smears (42.9%). Notably, SCC cases were perfectly identified by SCC PAP smears, with all such cases confirmed by histopathology. A Chi-Square test was conducted to evaluate the statistical significance of these distributions, yielding a Chi-Square value of 197.697 and a highly significant p-value of .0001 ($p < 0.01$). This result strongly indicates that the observed distributions are not due to random chance, underscoring a significant association between PAP smear results and histopathological diagnoses. The findings support the efficacy of PAP smears in detecting specific cervical conditions, while also highlighting areas for improvement, particularly in increasing the sensitivity for detecting SCC to ensure comprehensive screening and early diagnosis.

Table 2: Statistical Analysis

HPE diagnosis	Cytology diagnosis											Chi-Square	p-value	
	ASC-H		ASCUS		HSIL		LSIL		SCC		Total			
Chronic cervicitis	0	0.0 %	2	46.2 %	0	0.0 %	2	12.5 %	0	0.0 %	2	24.5 %	197.697	.0001**
Chronic cervicitis with squamous metaplasia	0	0.0 %	1	30.8 %	0	0.0 %	3	18.8 %	0	0.0 %	1	17.9 %		
HSIL	2	28.6 %	0	0.0 %	1	42.9 %	0	0.0 %	0	0.0 %	1	13.2 %		
LSIL	3	42.9 %	1	23.1 %	0	0.0 %	1	68.8 %	0	0.0 %	2	24.5 %		
Moderately differentiated SCC	0	0.0 %	0	0.0 %	1	39.3 %	0	0.0 %	0	0.0 %	1	10.4 %		
SCC	2	28.6 %	0	0.0 %	0	0.0 %	0	0.0 %	3	100.0 %	5	4.7 %		
Well-differentiated SCC	0	0.0 %	0	0.0 %	5	17.9 %	0	0.0 %	0	0.0 %	5	4.7 %		
Total	7	100.0 %	5	100.0 %	2	100.0 %	1	100.0 %	3	100.0 %	10	100.0 %		

DISCUSSION

The present study's findings underscore the utility and limitations of PAP smears in detecting various cervical lesions, particularly Squamous Cell Carcinoma (SCC). In line with Naik et al., our study also highlights a significant correlation between cytological findings and histopathological diagnoses, emphasizing the reliability of PAP smears for early detection of cervical abnormalities. Specifically, Naik et al. reported a sensitivity of 86.6% and specificity of 86.3% in their study¹. Similarly, Bhalerao et al. reported a high correlation between PAP smears, colposcopy, and histopathology in women with unhealthy cervix, which supports our findings of high specificity but lower sensitivity in detecting SCC. Bhalerao et al. observed a sensitivity of 87% and specificity of 94% for PAP smears in their study².

The detection rates of chronic cervicitis and chronic cervicitis with squamous metaplasia in our study mirror the findings of Hardeep et al., who observed similar patterns in a tertiary care hospital in Western Uttar Pradesh, India. Hardeep et al. reported sensitivity and specificity values of 71% and 98%, respectively, for PAP smears³. This consistency underscores the generalizability of our findings across different regional settings.

In evaluating HSIL and LSIL, Singh et al. highlighted the comparative effectiveness of colposcopy and cytology, which aligns with our results where HSIL and LSIL were effectively identified through PAP smears, albeit with varying degrees of sensitivity. Singh et al. found that PAP smears had a sensitivity of 70% and specificity of 95%⁴. The high specificity and positive predictive value (PPV) for SCC detection in our study are corroborated by Rani et

al., who emphasized the role of PAP smears in detecting premalignant and malignant lesions of the cervix. Rani et al. reported a sensitivity of 76% and a specificity of 95%⁵

Khan and Khan's study on cytomorphological patterns also aligns with our findings, particularly regarding the distribution of histopathological diagnoses across different PAP smear categories. Khan and Khan reported sensitivity and specificity values of 84% and 92%, respectively, for PAP smears⁶. Solanke et al. provided evidence of cytohistological correlation, which supports our study's findings on the significant association between PAP smear results and histopathological diagnoses. Solanke et al. reported a sensitivity of 80% and specificity of 97%⁷.

The retrospective studies by Bindroo and Garg, as well as Gupta et al., further reinforce the importance of correlating cytological findings with histopathology to enhance diagnostic accuracy. Bindroo and Garg reported a sensitivity of 85% and specificity of 93%⁸, while Gupta et al. reported a sensitivity of 75% and specificity of 89%⁹. Mittal and Mittal, along with Subechhya et al., have documented similar findings in their respective studies, highlighting the crucial role of cytological examination in cervical cancer screening and its histopathological confirmation. Mittal and Mittal reported sensitivity and specificity values of 78% and 96%, respectively¹⁰, while Subechhya et al. reported values of 82% and 94%¹¹.

Farooq et al. and Kumar et al. also reported on the significant correlation between cervical PAP smears and histopathological diagnoses, supporting our findings of high specificity and the need for improved sensitivity. Farooq et al. reported a sensitivity of 77% and specificity of 93%¹², while Kumar et al. reported values of 80% and 91%¹³. The studies by Sirasagi et al. and Malpani et al. further emphasize the accuracy of PAP smears in detecting abnormal epithelial lesions and their histopathological correlation, consistent with our results. Sirasagi et al. reported a sensitivity of 81% and specificity of 94%¹⁴, while Malpani et al. reported values of 79% and 96%¹⁵.

Lastly, Patil and Jibhkate, as well as Rajeswari et al., documented similar cytohistopathological correlations in their hospital-based studies, affirming the reliability of PAP smears in detecting cervical abnormalities and the importance of histopathological confirmation for accurate diagnosis. Patil and Jibhkate reported a sensitivity of 83% and specificity of 92%¹⁶ while Rajeswari et al. reported values of 85% and 94%¹⁷.

CONCLUSION

The findings of this study align with a broad body of literature that underscores the effectiveness of PAP smears in cervical cancer screening, particularly in confirming the presence of SCC. However, the lower sensitivity for detecting all SCC cases highlights an area for potential improvement in screening protocols, as corroborated by various studies in the field.

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CONFLICT OF INTEREST:- The authors have no conflict of interest and nothing to declare.

AUTHOR CONTRIBUTIONS:-

R SOWMYA and *SRIDEVI M* contemplated the visualization, conceptualization, and project administration of the study. *R SOWMYA* aided in writing original draft preparation and data curation. *SRIDEVI M* advocated validation and formal analysis. All authors endorsed manuscript revision and have certified the submitted manuscript.

REFERENCES

1. Naik R, Minj AM, Panda R, Satpathi S, Behera PK, Panda KM. Cytohistological correlation and accuracy of the pap smear test in diagnosis of cervical lesions: a hospital based cross-sectional study from Odisha, India. *Medical Science*. 2015 Sep 30;3(3):242-9.
2. Bhalerao A, Kulkarni S, Ghike S, Kawthalkar A, Joshi S. Correlation of pap smear, colposcopy and histopathology in women with unhealthy cervix. *J South Asian Feder Obst Gynae*. 2012 May;4(2):97-8.
3. Hardeep K, Alka S, Rajendra T. Study of cervical PAP smears in a tertiary care hospital of western Uttar Pradesh, India. *J Cytol*. 2015;32(2):70-3.
4. Singh N, Seth S, Mehta S, Sharma A, Bhalla P. A comparative study of colposcopy and cytology in evaluation of unhealthy cervix. *J Midlife Health*. 2015;6(2):78-83.

5. Rani R, Mittal M, Kumar R. Role of Pap smear in detecting premalignant and malignant lesions of cervix. *Trop J Pathol Microbiol.* 2021;7(4):164–8.
6. Khan MA, Khan A. Cytomorphological patterns of cervical PAP smears and its correlation with clinical findings. *Int J Health Sci Res.* 2021;11(6):122–7.
7. Solanke P, Patil G, Desai S. Cytohistological correlation of cervical lesions. *Int J Health Sci Res.* 2020;10(7):153–8.
8. Bindroo S, Garg M. Correlation of cervical pap smear with histopathological diagnosis in cervical lesions: A 2 years retrospective study.
9. Gupta R, Gupta A, Gupta RK. Cytomorphological analysis of cervical PAP smears in symptomatic women. *J Cytol.* 2019;36(1):10–4.
10. Mittal R, Mittal N. Cervical cytology and histopathological correlation in unhealthy cervix. *Int J Health Sci Res.* 2022;12(1):98–104.
11. Subechhya J, Binita G, Ekta J. Correlation of Cervical Pap Smear with Histopathological Diagnosis in Cervical Lesions.
12. Farooq R, Quraishi A, Mohammad S. Correlation of cervical pap smears with histopathological diagnosis in cervical lesions.
13. Kumar DS, Rajeswari K, Krishna R, Meenakshisundaram K. A retrospective study of pap smear and cervical biopsy correlation in abnormal cervical cytology cases.
14. Sirasagi A, Arpitha K, Neeha S, Pattar PM. A two year retrospective study of cytohistopathological correlation of cervical smear in a tertiary care hospital.
15. Malpani G, Agrawal P, Varma AV, Khandelwal N, Tignath G. Cervical Pap smear study and detection of abnormal epithelial lesions and determination of its accuracy by cytohistological correlation in patients of tertiary care teaching hospital in central India.
16. Patil PR, Jibhkate SN. Cytohistopathological correlation of Papanicolaou smears: a hospital-based study.
17. Rajeswari R, Chandulee KS, Suneetha K, Prasanna BP. Cytohistological Correlation of Cervical PAP Smears - A Two Year Retrospective Study from Ongole, Andhra Pradesh.