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Original Research Article

Diagnostic Correlation of Cervical Cytology and Biopsy Findings Using the Bethesda System

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Abstract

Background: Cervical cancer remains a major public health problem, particularly in developing countries, despite the availability of effective screening methods. The Papanicolaou (Pap) smear, reported using the Bethesda System, is widely used for early detection of cervical lesions, while histopathological examination of biopsy specimens serves as the gold standard for diagnosis. Correlation between cytology and histopathology is essential to assess the diagnostic accuracy of Pap smear.

Objectives: To evaluate the cytohistopathological correlation of cervical lesions using the Bethesda System and to determine the diagnostic performance of Pap smear in comparison with histopathology.

Methods: This hospital-based cross-sectional analytical study included 170 women who underwent both Pap smear and cervical biopsy. Cytological findings were reported according to the Bethesda System, and histopathological diagnoses were categorized as benign lesions, CIN I, CIN II, CIN III, and carcinoma. Histopathology was considered the gold standard. Statistical analysis included calculation of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy. Agreement between cytology and histopathology was assessed using the kappa statistic.

Results: The majority of patients were in the 40–49 years age group (38.8%), with vaginal discharge being the most common presenting complaint (51.8%). On cytology, LSIL (22.4%) was the most common abnormal finding, followed by HSIL (17.6%). Histopathology revealed benign lesions in 32.9% cases, while CIN I, CIN II, and CIN III accounted for 23.5%, 17.6%, and 14.1% cases, respectively, with carcinoma in 11.8%. Cytohistological correlation showed that LSIL corresponded predominantly to CIN I, while HSIL correlated with CIN II and CIN III. The Pap smear demonstrated a sensitivity of 92.98%, specificity of 71.43%, PPV of 86.89%, NPV of 83.33%, and overall diagnostic accuracy of 85.88%. The kappa coefficient of 0.61 indicated substantial agreement.

Conclusion: Pap smear is a highly sensitive and effective screening tool for the detection of cervical lesions; however, histopathological examination remains essential for definitive diagnosis. Cytohistological correlation improves diagnostic accuracy and helps in appropriate patient management.

Keywords: Pap Smear, Bethesda System, Cervical Cancer, Cytohistological Correlation, CIN, Diagnostic Accuracy.

Introduction

Cervical cancer remains one of the most common malignancies affecting women worldwide, particularly in low- and middle-income countries, where it contributes significantly to morbidity and mortality [1]. Persistent infection with high-risk types of human papillomavirus (HPV), especially HPV 16 and 18, is recognized as the primary etiological factor in the development of cervical intraepithelial neoplasia (CIN) and invasive carcinoma [2]. Despite being largely preventable through effective screening and vaccination strategies, cervical cancer continues to pose a major public health challenge due to inadequate screening coverage, late diagnosis, and limited access to healthcare services in many regions [3].

The Papanicolaou (Pap) smear has long been established as a cornerstone of cervical cancer screening, enabling early detection of premalignant and malignant lesions [4]. To standardize reporting and improve diagnostic accuracy, the Bethesda System (TBS) was introduced and later revised, providing a uniform terminology for cytological

interpretation, including categories such as atypical squamous cells (ASC), low-grade squamous intraepithelial lesions (LSIL), high-grade squamous intraepithelial lesions (HSIL), and carcinoma [5]. This system not only facilitates communication between cytopathologists and clinicians but also guides patient management and follow-up protocols [6].

Histopathological examination of cervical biopsy specimens remains the gold standard for definitive diagnosis and grading of cervical lesions [7]. Correlation between cytological findings based on the Bethesda System and histopathological outcomes is essential to evaluate the diagnostic performance, sensitivity, specificity, and predictive value of Pap smear screening [8]. Such correlation studies help identify discrepancies, reduce false-negative and false-positive rates, and improve overall screening effectiveness [9]. Therefore, this study aims to analyze the concordance between Pap smear findings categorized by the Bethesda System and histopathological diagnoses in cervical lesions, thereby assessing the reliability of cytology as a screening tool in clinical practice.

Methodology

This was a hospital-based cross-sectional analytical study conducted in the Department of Pathology in collaboration with the Department of Obstetrics and Gynecology at a tertiary care teaching hospital. The study included women presenting with symptoms such as abnormal vaginal discharge, postcoital bleeding, intermenstrual bleeding, or those undergoing routine cervical cancer screening. All eligible patients who underwent both Pap smear examination and subsequent cervical biopsy during the study period were included. Patients with prior treatment for cervical intraepithelial lesions or carcinoma, pregnant women, and those with inadequate cytology smears were excluded. Cervical samples for cytology were collected using an Ayre's spatula and/or endocervical brush, fixed in alcohol, and stained using the Papanicolaou technique. Cytological findings were reported according to the Bethesda System, classifying lesions into categories such as NILM, ASC-US, ASC-H, LSIL, HSIL, and carcinoma [5].

Subsequently, cervical biopsy specimens were obtained from the same patients under colposcopic guidance or clinical indication and processed for histopathological examination using standard paraffin-embedding and hematoxylin and eosin staining. Histopathological diagnosis was considered the gold standard and categorized into benign lesions, CIN I, CIN II, CIN III, and invasive carcinoma as per WHO classification [7]. The sample size was calculated using Buderer's formula for diagnostic accuracy studies, assuming an expected sensitivity of 80%, 95% confidence level, 10% precision, and a prevalence of 40%, yielding a minimum sample size of 154, which was increased to 170 to account for inadequate samples. Data were entered in Microsoft Excel and analyzed using SPSS software. Statistical measures including sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of Pap smear were calculated. The agreement between cytological and histopathological findings was assessed using the kappa statistic, with a p-value <0.05 considered statistically significant.

Results

Table 1: Socio-demographic and clinical profile of study participants (n = 170)

Variable	Frequency	Percentage (%)
Age group (years)		
<30	22	12.9
30–39	46	27.1
40–49	66	38.8
≥50	36	21.2
Parity		
Nulliparous	18	10.6
Multiparous	152	89.4
Predominant presenting complaint		
Vaginal discharge	88	51.8
Postcoital bleeding	16	9.4
Intermenstrual bleeding	22	12.9
Postmenopausal bleeding	14	8.2
Lower abdominal pain	18	10.6
Asymptomatic / routine screening	12	7.1

The present study included 170 women, with the majority belonging to the age group of 40–49 years (38.8%), followed by 30–39 years (27.1%). Women aged ≥50 years constituted 21.2%, while only 12.9% were below 30 years. This indicates that cervical lesions were more commonly detected in the middle-aged population, which is consistent with the natural history of HPV-related disease progression

[10]. A large proportion of the study population was multiparous (89.4%), highlighting the known association between high parity and increased risk of cervical neoplasia [11]. The most common presenting complaint was vaginal discharge (51.8%), followed by intermenstrual bleeding (12.9%) and lower abdominal pain (10.6%). Postcoital bleeding and postmenopausal bleeding were observed in 9.4% and 8.2% cases, respectively, while 7.1% of women were asymptomatic and detected during routine screening. These findings are comparable with other hospital-based studies where symptomatic women predominate [12].

Table 2: Distribution of Pap smear findings according to the Bethesda system (n = 170)

Cytology category	Frequency	Percentage (%)
NILM / benign inflammatory smear	48	28.2
ASC-US	22	12.9
ASC-H	12	7.1
LSIL	38	22.4
HSIL	30	17.6
Squamous cell carcinoma	20	11.8
Total	170	100.0

Cytological evaluation using the Bethesda System revealed that 28.2% of cases were reported as NILM (negative for intraepithelial lesion or malignancy). Among abnormal smears, LSIL was the most common finding (22.4%), followed by HSIL (17.6%), ASC-US (12.9%), ASC-H (7.1%), and squamous cell carcinoma (11.8%). The relatively higher proportion of epithelial cell abnormalities in this study can be attributed to the inclusion of clinically suspected cases undergoing biopsy, rather than a general screening population [13]. The distribution pattern aligns with previous studies where LSIL and HSIL constitute the majority of abnormal cytological findings [14].

Table 3: Histopathological diagnosis of cervical lesions (n = 170)

Histopathology diagnosis	Frequency	Percentage (%)
Chronic cervicitis / benign lesion	56	32.9
CIN I	40	23.5
CIN II	30	17.6
CIN III	24	14.1
Invasive squamous cell carcinoma	20	11.8
Total	170	100.0

Histopathological examination, considered the gold standard, showed that 32.9% of cases had benign lesions such as chronic cervicitis. Among premalignant lesions, CIN I was the most common (23.5%), followed by CIN II (17.6%) and CIN III (14.1%). Invasive carcinoma was observed in 11.8% of cases.

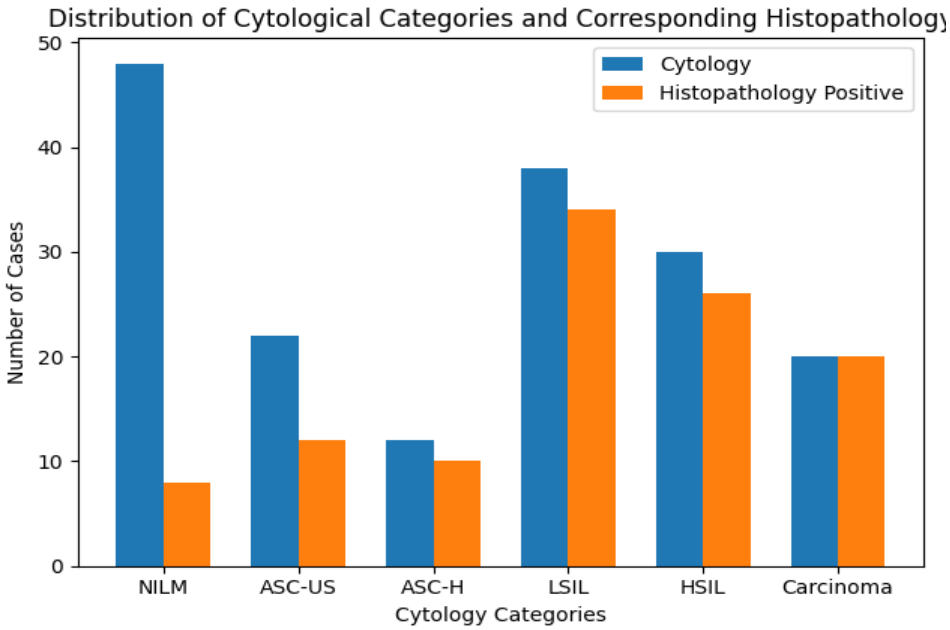

Figure 1: Distribution of Cytological Categories and Corresponding Histopathology

This distribution reflects a typical progression pattern from low-grade to high-grade lesions and carcinoma and is consistent with studies conducted in tertiary care settings where a higher proportion of premalignant and malignant lesions are encountered [10]. The relatively high prevalence of CIN and carcinoma underscores the importance of timely screening and early diagnosis [12].

Table 4: Correlation between Pap smear findings and histopathology (n = 170)

Cytology ↓ / Histopathology →	Benign	CIN I	CIN II	CIN III	Carcinoma	Total
NILM / benign inflammatory smear	40	6	2	0	0	48
ASC-US	10	8	3	1	0	22
ASC-H	2	2	4	3	1	12
LSIL	4	20	8	4	2	38
HSIL	0	4	12	10	4	30
Squamous cell carcinoma	0	0	1	6	13	20
Total	56	40	30	24	20	170

A detailed cytohistological correlation demonstrated that most NILM cases corresponded to benign histology (40 out of 48), although a small number showed underlying CIN, indicating possible false-negative cytology. ASC-US cases showed variable histopathological outcomes, ranging from benign lesions to CIN II and III, reflecting its heterogeneous nature.

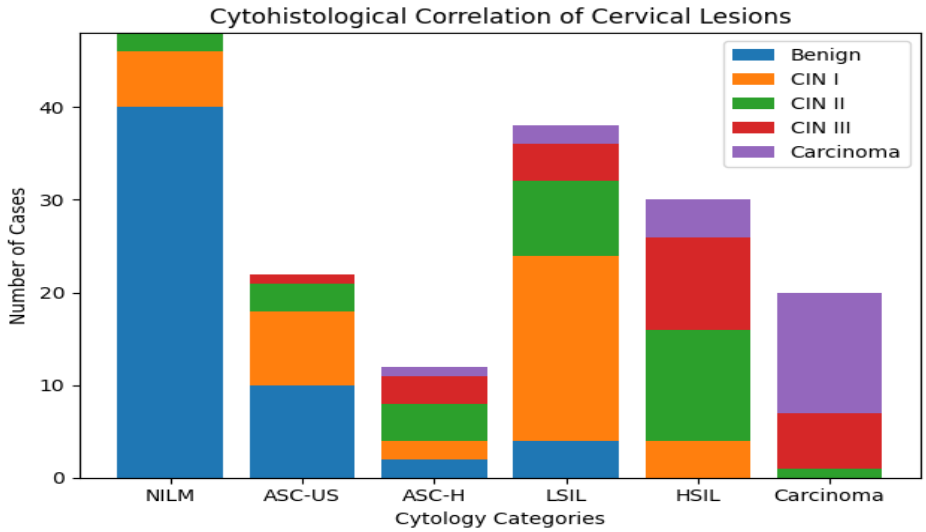

Figure 2: Cytohistological Correlation of Cervical Lesions

LSIL cases correlated predominantly with CIN I (20 out of 38), while HSIL cases showed strong association with CIN II and CIN III (22 out of 30). Cytological diagnosis of carcinoma showed high concordance with histopathological carcinoma (13 out of 20 cases), although a few cases were underdiagnosed as high-grade lesions. Overall, the correlation demonstrates a progressive increase in lesion severity from lower to higher cytological categories, supporting the validity of the Bethesda System while also highlighting areas of discrepancy [14][15].

Table 5: Diagnostic accuracy of Pap smear using histopathology as gold standard

Parameter	Value
Sensitivity	92.98%
Specificity	71.43%
Positive Predictive Value (PPV)	86.89%
Negative Predictive Value (NPV)	83.33%
Overall diagnostic accuracy	85.88%

Using histopathology as the gold standard and considering ASC-US and above as positive cytology, the Pap smear demonstrated a sensitivity of 92.98% and specificity of 71.43%. The positive predictive value was 86.89%, and the negative predictive value was 83.33%, with an overall diagnostic accuracy of 85.88%. The high sensitivity indicates that Pap smear is an effective screening tool for detecting cervical lesions, whereas the relatively lower specificity suggests the possibility of false-positive results, which is acceptable in a screening context where early detection is prioritized [10]. These findings are comparable with

other studies reporting high sensitivity but variable specificity of Pap smear [13].

Table 6: Agreement between cytology and histopathology

Statistic	Value
Kappa coefficient	0.61
Standard error	0.07
p-value	<0.001
Interpretation	Substantial agreement

The agreement between cytological and histopathological findings was assessed using the kappa statistic, which showed a value of 0.61, indicating substantial agreement. The result was statistically significant ($p < 0.001$), confirming that the correlation between Pap smear and biopsy findings was not due to chance. This level of agreement is consistent with previously reported studies, where kappa values typically range from moderate to substantial due to inherent limitations such as sampling errors, observer variability, and lesion heterogeneity [16]. The findings reinforce the reliability of cytology as a screening tool while emphasizing the need for histopathological confirmation.

Discussion

The present study evaluated the cytohistopathological correlation of cervical lesions using the Bethesda System and histopathology as the gold standard. The majority of patients in this study belonged to the 40–49 years age group, which is consistent with the known natural history of cervical carcinogenesis, where persistent HPV infection progresses to premalignant and malignant lesions over several years [10]. Multiparity was observed in a large proportion of cases, supporting its role as an established risk factor for cervical neoplasia due to repeated cervical trauma and increased susceptibility to HPV infection [11]. The predominance of symptoms such as vaginal discharge and abnormal bleeding in this study aligns with findings from other hospital-based studies, where symptomatic patients are more likely to undergo further diagnostic evaluation including biopsy [12].

The cytological distribution in this study showed that LSIL and HSIL constituted a significant proportion of abnormal smears, with LSIL being the most common abnormality. This pattern is comparable to other tertiary care studies, where the prevalence of epithelial abnormalities is higher due to selective inclusion of clinically suspected cases rather than routine screening populations [13]. The proportion of HSIL and carcinoma cases in the present study further emphasizes the importance of early screening, as these categories are associated with a higher risk of progression to invasive cancer if left untreated [14]. The use of the Bethesda System ensured standardized reporting and facilitated effective communication between clinicians and pathologists [5].

Histopathological examination revealed that a considerable number of cases were diagnosed as CIN I, followed by CIN II and CIN III, with invasive carcinoma accounting for a smaller but significant proportion. This distribution reflects the typical progression of cervical lesions and is comparable with other studies conducted in similar settings [10]. The cytohistological correlation demonstrated that lower-grade cytological abnormalities such as LSIL were predominantly associated with CIN I, whereas HSIL showed strong correlation with CIN II and CIN III. However, some discrepancies were observed, including underdiagnosis in NILM and overdiagnosis in certain ASC categories, which may be attributed to sampling errors, inflammatory changes, or observer variability [14][15]. These findings highlight the inherent limitations of cytology and the need for confirmatory histopathological evaluation.

The diagnostic performance of Pap smear in the present study showed high sensitivity (92.98%) and moderate specificity (71.43%), with an overall accuracy of 85.88%. These findings are in agreement with previously published studies, where Pap smear is recognized as a highly sensitive screening tool but with variable specificity depending on study design and population [13]. The kappa value of 0.61 indicated substantial agreement between cytology and histopathology, which is consistent with earlier reports demonstrating moderate to substantial concordance [16]. The relatively lower specificity and presence of false-positive and false-negative cases underscore the importance of adjunctive methods such as HPV testing and colposcopy to improve diagnostic accuracy. Overall, the study reinforces the utility of Pap smear as an effective screening modality while emphasizing the critical role of biopsy for definitive diagnosis.

References

1. World Health Organization. Cervical cancer. Geneva: WHO.
2. International Agency for Research on Cancer. Human papillomavirus and cervical cancer. Lyon: IARC.

3. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics: GLOBOCAN estimates. CA Cancer J Clin. 2018;68(6):394–424. doi:10.3322/caac.21492.
4. Papanicolaou GN, Traut HF. Diagnosis of uterine cancer by the vaginal smear. New York: Commonwealth Fund; 1943.
5. Nayar R, Wilbur DC. The Bethesda System for Reporting Cervical Cytology. Springer; 2015. doi:10.1007/978-3-319-11074-5.
6. Solomon D, Davey D, Kurman R, Moriarty A, O'Connor D, Prey M, et al. The Bethesda System terminology. JAMA. 2002;287(16):2114–2119. doi:10.1001/jama.287.16.2114.
7. Kurman RJ, Carcangiu ML, Herrington CS, Young RH. WHO classification of tumours of female reproductive organs. IARC; 2014.
8. Stoler MH, Schiffman M. Interobserver reproducibility of cervical cytology. JAMA. 2001;285(11):1500–1505. doi:10.1001/jama.285.11.1500.
9. Koss LG. Diagnostic cytology and its histopathologic bases. Lippincott Williams & Wilkins; 2006.
10. Barut MU, Kale A, Kuyumcuoğlu U, Bozkurt M, Ağar M, Doğan Gün B, et al. Analysis of smear and colposcopy in cervical lesions. Med Sci Monit. 2015;21:1254–1260. doi:10.12659/MSM.893135.
11. Saha R, Thapa M. Correlation of cervical cytology with histology. Kathmandu Univ Med J. 2005;3(3):222–224.
12. Gothwal M, et al. Spectrum of abnormal cervical lesions and cytohistological correlation. J Cytol. 2016;33(3):149–153. doi:10.4103/0970-9371.188050.
13. Belekar SV, et al. Cervical cytology and histology correlation. J Cytol. 2019;36(2):83–87. doi:10.4103/JOC.JOC_176_17.
14. Asaturova A, et al. Cervical cytology-histology correlation. Cancer Cytopathol. 2020;128(6):405–417. doi:10.1002/cncy.22253.
15. Mukhopadhyay S, et al. Evaluation of HSIL category in Bethesda system. Cytojournal. 2011;8:4. doi:10.4103/1742-6413.76595.
16. Nayar R, Wilbur DC. Bethesda System: historical perspective. Acta Cytol. 2017;61(4-5):359–372. doi:10.1159/000477556.