International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Bharaswadkar G et al. Int J Reprod Contracept Obstet Gynecol. 2025 May;14(5):1389-1394
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20251215

Original Research Article

Agreement between cytology, colposcopy and histopathology in assessment of precancerous cervical lesions

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Received: 24 October 2024
Revised: 04 January 2025
Accepted: 13 January 2025

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ABSTRACT

Background: Cervical cancer ranks as the third most common gynaecologic cancer in the world. The incidence rate for cervical cancer in Australia is 7.1 cases per 100,000 females as per 2022 data. Reduction in cervical cancer morbidity and mortality is based on the early detection of premalignant lesions. The aim of this clinical audit was to evaluate the agreement between the histology findings and CST LBC results/colposcopy impression in assessment of precancerous cervical lesions in all patients referred for colposcopy in view of abnormal cervical cytology.
Methods: This retrospective study included 108 participants. The study was conducted from June 2022 to May 2023 at blinded for review method. Cervical biopsy was performed on 48 cases out of the total 108 women based on colposcopy findings. The significance of the association between CST LBC result and colposcopy impression with histology of biopsy specimen was performed using the Chi-square test or Fisher's exact.
Results: More than two-thirds of the colposcopy impressions (n=22/32, 68.75%) indicated LSIL matched the results of the biopsy findings. More than 80% of the CST results indicating HSIL (n=14/16, 87.50%) matched biopsy findings. Two-thirds of the CST results (n=14) indicated LSIL matched the results of the biopsy findings. The weighted Kappa measure for agreement between CST LBC result and biopsy findings was 0.464, 95% CI: 0.20-0.73.
Conclusions: Correlation of CST LBC result and colposcopy with histopathology, as the diagnostic tool in this study, was significant ($p<0.001$) Combination of cytology and colposcopy helped in the successful identification of pre-malignant lesions.

Keywords: Cervix biopsy, Colposcopy, CST, HPV, HSIL, LSIL

INTRODUCTION

Cervical cancer ranks as the third common gynaecologic cancer in the world.[1] Incidence rate for cervical cancer in Australia is 7.1 cases per 100,000 females as per 2022 data.[2] Reduction in cervical cancer morbidity and mortality is based on the early detection of premalignant lesions. Improved screening through cervical cytology and human papillomavirus (HPV) testing methods have decreased cervical cancer incidence.[3]

The objective of performing colposcopy following an abnormal cervical screening test result is to assess the nature, severity, and extent of this abnormality.[4]

A previous study had mentioned that colposcopy impression very closely correlated with the cytology diagnosis and combination of the two produced optimum results.[5]

In both Australia and New Zealand, cervical screening is conducted as per the guidelines set by a National Cervical

Screening Program (NCSP). The guidelines incorporate the outcome of a thorough review of evidence and expert advice from professionals in the field of medicine, epidemiology and also from consumer representatives.

The National Cervical Screening Program in Australia changed in 2017 from 2 yearly cervical cytology testing to 5 yearly primary HPV screening with reflex liquid-based cytology for women in whom high risk oncogenic HPV type is detected.

The present study aimed to evaluate the performance of colposcopy examination in our unit by examining the correlation between cytology (Bethesda 2001 terminology) with cervical biopsy histopathology findings and colposcopy findings correlation with cervical biopsy histopathology findings for the early detection of premalignant cervical lesions.

Objectives

The aim of this clinical audit was to evaluate the agreement between the histology findings and CST LBC results/colposcopy impression in assessment of precancerous cervical lesions in all patients referred for colposcopy in view of abnormal cervical cytology.

METHODS

Type of study

The study was a retrospective study.

Study participants

This study included 108 women who underwent colposcopy for abnormal cervical cytology between June 2022 and May 2023 at Hornsby Ku-ring-gai Hospital.

Out of 108 women, cervix biopsy was done in 48 cases based on colposcopy assessment. Patients with the following abnormal cytology types were included in the study: HPV 16/18/non16, 18 positives, negative for squamous intra-epithelial lesion, LSIL (low-grade squamous intraepithelial lesion), HSIL (high-grade squamous intraepithelial lesion) and invasive cancer. All patients had a colposcopy examination and cervix biopsy if necessary. We only included the above-mentioned lesions to simplify statistical agreement

Agreement between the histology findings and CST LBC results/colposcopy impression was assessed. Also, colposcopy impression was correlated with cervix biopsy histopathology.

Inclusion criteria

The study included women who underwent colposcopy for abnormal cervical screening test-HPV high risk type 16/18/others detected; cases in which cervix biopsy was done.

Exclusion criteria

Normal CST; normal colposcopy; unsatisfactory colposcopy cases were excluded.

Colposcopy examination

Cytology results were classified as negative for squamous intra-epithelial lesion, LSIL, HSIL. Colposcopies were performed for all of the included patients.

Cervix biopsy was done in cases having abnormal features on colposcopy.

Colposcopic examination was done as per standard established protocol: cervical examination for any gross lesion without preparation, green filter examination for abnormal vascular pattern and application of 5% acetic acid for identifying any abnormal aceto-white areas.

The colposcopic data results were coded as negative, low-grade lesions, high-grade lesions, or invasive lesions.

Interpretation of cervical biopsy specimens was done as per standard histologic criteria. All pathological lesions were classified as low-grade squamous intra-epithelial lesions, high-grade squamous intra-epithelial lesions, or carcinoma. After histopathology diagnosis of cervix biopsy specimen, patients were managed as per the NCSP guidelines.

The main outcome of the study was agreement between the histology findings and CST LBC results/colposcopy impression.

Statistical analysis

The data on CST LBC results, colposcopy impressions, and histology of biopsy specimens were presented using frequency and contingency tables and bar plots. The significance of the association between CST result and colposcopy impression with histology of biopsy specimen was performed using the Chi-square test or Fisher's exact test to account for sparsely distributed data. The magnitude and significance of the agreement between CST LBC results, and colposcopy impressions with histology was assessed using a weighted Kappa measure based on linear and quadratic weights.

All the statistical tests were performed at a 0.05 level of significance. The statistical analysis was performed in STATA, version 17.0.

RESULTS

Table 1 shows the contingency table of CST LBC results and cervical biopsy histology findings. The CST LBC

result showed the maximum impressions on HSIL (82.35%). LSIL impressions were found to be at a maximum of 80% and a minimum of 11.76%.

Table 2 illustrates the contingency table of colposcopy impressions and cervical biopsy histology findings. More than two-thirds of the colposcopy impressions (n=22/32, 68.75%) indicated LSIL matched the results of the biopsy findings. More than 80% of the CST results indicating HSIL (n=14/16, 87.50%) matched biopsy findings. There was a statistically significant association between the two findings (p≤0.001).

Table 3 presents the corresponding bar plot. Two-thirds of the CST results (n=14) indicated LSIL matched the results of the biopsy findings. More than 80% of the CST results indicating HSIL (n=14, 82.35%) matched biopsy findings. There was a statistically significant association between the two findings (p≤0.001).

Table 1: Association of cervical cytology with cervical biopsy histopathology findings.

CST LBC Result	Histology of biopsy specimen			
	Negative	LSIL	HSIL	Carcinoma
Negative	0 (0.0) [0.0]	8 (80.00) [33.33]	2 (20.00) [10.00]	0 (0.00) [0.00]
LSIL	3 (14.29) [100.0]	14 (66.67) [58.33]	4 (19.05) [20.00]	0 (0.0) [0.00]
HSIL	0 (0.00) [0.0]	2 (11.76) [8.33]	14 (82.35) [70.00]	1 (5.88) [100]

Note: values within open parenthesis are percentages to the row total; values within the square brackets are percentages to the column total.

Table 2: Association of colposcopy with cervical biopsy histopathology findings.

Colposcopy impression	Histology of biopsy specimen		
	Negative	LSIL	HSIL
LSIL	2 (6.25) [100.0]	22 (68.75) [8.33]	8 (25.00) [36.36]
HSIL	0 (0.00) [0.0]	2 (12.50) [91.67]	14 (87.50) [63.64]

Note: values within open parenthesis are percentages to the row total; values within the square brackets are percentages to the column total.

Table 3: Association of cervical cytology with cervical biopsy histopathology findings.

CST LBC result	Histology of biopsy specimen			
	Negative	LSIL	HSIL	Carcinoma
Negative	0 (0.0) [0.0]	8 (80.00) [33.33]	2 (20.00) [10.00]	0 (0.00) [0.00]
LSIL	3 (14.29) [100.0]	14 (66.67) [58.33]	4 (19.05) [20.00]	0 (0.0) [0.00]
HSIL	0 (0.00) [0.0]	2 (11.76) [8.33]	14 (82.35) [70.00]	1 (5.88) [100]

Note: values within open parenthesis are percentages to the row total; values within the square brackets are percentages to the column total.

Table 4: Association of colposcopy with cervical biopsy histopathology findings.

Colposcopy impression	Histology of biopsy specimen		
	Negative	LSIL	HSIL
LSIL	2 (6.25) [100.0]	22 (68.75) [8.33]	8 (25.00) [36.36]
HSIL	0 (0.00) [0.0]	2 (12.50) [91.67]	14 (87.50) [63.64]

Note: values within open parenthesis are percentages to the row total; values within the square brackets are percentages to the column total.

The weighted Kappa measure for agreement between CST LBC result and biopsy findings was 0.464, 95% CI: 0.20-0.73. The corresponding Kappa measure for colposcopy impressions and biopsy findings was 0.177, 95% CI: 0.09-0.27. When linear weights were used, the Kappa measure for CST LBC and biopsy findings was 0.387 and it was 0.0.25 for colposcopy impression and biopsy findings. Using the guidelines for interpretation proposed by Landis and Koch, these results indicate a moderate level of agreement between CST LBC results and biopsy findings, and only slight agreement between colposcopy impression and biopsy findings.

Table 4 indicates the association of the colposcopy with the biopsy done on the cervix histopathological findings. HSIL was at a maximum of 87.5%, whereas LSIL was at 25%.

Significant associations were observed between both CST LBC and colposcopy findings when compared to biopsy results. There was a moderate level of agreement between CST LBC results and biopsy findings. The agreement level between colposcopy impressions and biopsy findings was low.

DISCUSSION

This study showed that there was a statistically significant association between CST LBC result and cervix biopsy as well as between colposcopy impression and cervix biopsy. Significant associations were observed between both CST LBC and colposcopy findings when compared to biopsy results.

Benedet et al has concluded in their study that colposcopy is highly accurate in diagnosing high grade lesions. They have also mentioned that colposcopy impression very closely correlated with the cytology diagnosis and combination of the two produced optimum results.[5] Our study showed an 87% correlation in colposcopy findings of HSIL with confirmation on cervical biopsy in the HSIL group, 13% however labelled as HSIL on colposcopy were diagnosed as LSIL after cervical biopsy. LSIL was the correct colposcopy impression in 69% of patients in the LSIL group however 25% labelled as LSIL on colposcopy were found to be HSIL on cervical biopsy.

Tamiolakis et al concluded in their study that an integrated cytology-colposcopy program assisted effectively in reaching the diagnosis of an abnormal cervical pathological condition. The concurrent use of cytological studies and colposcopy has been shown to enhance detection of the cervical cancer detection.[6]

Colposcopy involves assessment and typing of the transformation zone (TZ), identification of any gross abnormalities, and focussed biopsies of abnormal areas to exclude invasive disease.[7]

In both Australia and New Zealand, cervical screening is conducted as per the guidelines set by a National Cervical Screening Program (NCSP).[8] The guidelines incorporate the outcome of a thorough review of evidence and expert advice from professionals in the field of medicine, and epidemiology and also from consumer representatives.

In our study, LSIL was correctly identified on CST LBC in 67% while 19% patients of HSIL were missed on CST LBC screen. 82% patients with HSIL were correctly identified on CST LBC while 11.8% cases of LSIL were incorrectly labelled as HSIL and more importantly 6% diagnosed as HSIL on CST LBC had carcinoma of the cervix diagnosed following a directed biopsy.

Correct identification of LSIL was similar in both CST LBC (67%) and colposcopy group (69%). HSIL identification was higher following colposcopy (87%) as compared to CST LBC (82%) as expected however 6% of patients identified with HSIL on CST LBC were diagnosed with carcinoma of the cervix following colposcopy directed biopsy. Combined use of CST LBC and colposcopy to screen patients for presence of cervical cancer is an effective strategy however we identified the need to train our clinicians to identify HSIL changes in the cervix, at colposcopy.

In a study done by Katz et al it was found that the agreement was better between cytology and histopathology than between colposcopy and cytology or between colposcopy and histopathology.[9] When the colposcopy and histopathology were compared with respect to the colposcopy performed, there was a Kappa of 0.41 (95% CI=0.29-0.530) which can be considered as a moderate agreement.[9]

Akhter et al concluded in their study a strong agreement between histopathological and colposcopic findings. The study further went on to identify that the cytological findings with respect to colposcopy as well as histopathology remained weak.[10]

In a study, it was shown that colposcopy showed a good correlation with histopathology findings for proper evaluation of premalignant lesions which totally removes the need of a Pap smear.[11] Combined approach was preferred in these cases.[11]

Schulmeyer et al studied the correlation between cytology and colposcopy guided cytology for detecting cervical neoplasia in its earlier stages. Very severe lesions were detected accurately with colposcopy-guided Pap smears correlated to histopathology as compared to cytological findings without colposcopy.[12]

Jyothi et al concluded in their study that various viable methods when combined for a more accurate diagnostic purpose can lead to reduced mortality as well. The correlation between cytology, colposcopy and histopathology when used in combination provided better results as compared to when used individually.[13]

The amalgamated use of cytology and colposcopy screening in the early detection of cervical cancer has been proven to show much promise in a study done by Gupta et al. This diagnostic combination has helped many gynecologists to evaluate the uterine cervix efficiently, as revealed in the study.[14]

A study done by Bhalerao et al showed that correlation studies help in early diagnosis, thereby decreasing the morbidity and mortality of patients with cervix carcinoma.[15]

In another study, it was established that inflammatory changes in study participants were observed in colposcopic examinations which were often missed while performing standard cytological screenings. So, it was

enunciated that only standard procedures were not sufficient.[16]

Gadre SS et al proclaimed that Pap smear if combined with colposcopy screening in patients, it significantly increased the diagnostic yield and provided accurate and early diagnosis as well.[17]

Another similar study showcased that Pap smear findings greatly improved when correlated with cervical histology reports.[18]

The limitation of this study is there was low evidence to suggest that the agreement between colposcopy impressions and biopsy findings was comparable to that observed with CST LBC results and biopsy findings. This may be secondary to variations in the experience and skill levels of clinicians performing colposcopies. Another limitation of this study was that the sample size was small.

CONCLUSION

Correlation of CST LBC result and colposcopy with histopathology, as the diagnostic tool in this study, was significant ($p<0.001$) Combination of cytology and colposcopy helped in the successful identification of pre-malignant lesions. Even though the agreement level between colposcopy impressions and biopsy findings was lower as compared to that between CST LBC results and biopsy findings, there was a significant independent association of each screening test with biopsy findings.

Recommendations

Future research endeavours should aim for larger sample sizes and consider covariate adjustments for more robust conclusions.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Bharaswadkar G, Vatsayan A, Bhagavath V. Agreement between cytology, colposcopy and histopathology in assessment of precancerous cervical lesions. Int J Reprod Contracept Obstet Gynecol 2025;14:1389-94.