

Correlation of colposcopic examination results with histopathological findings and its diagnostic value in cervical biopsy

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Received 22 January 2023, Accepted for publication 10 May 2023

Abstract

Background & Aims: Cervical cancer is the fourth most frequently diagnosed cancer in women. Colposcopy is a worldwide accepted method for detection of early carcinoma of cervix. This study was conducted to investigate the correlation between colposcopic examination results with histopathological findings and its diagnostic value in cervical biopsy.

Materials & Methods: This study was a cross-sectional comparative study performed on 436 women with abnormal Pap smear test results, referring to Urmia Motahari Hospital during March 2021 to March 2022. Colposcopy and histopathologic findings of individuals with abnormal Pap smear results were extracted from the patient records. The data were analyzed using descriptive and analytic statistics (Chi-square test) using SPSS 21 (SPSS Inc., Chicago, IL.,USA). The sensitivity, specificity, and positive and negative predictive values of various diagnostic methods were calculated. A probability of $P < 0.05$ was accepted as significant.

Results: The mean age of the participants was 37.3 ± 9.60 . The most common finding in colposcopy and histopathology results were acetowhite lesions and cervicitis, respectively. According to the comparison, the agreement percentage of colposcopy and histopathology findings in noninvasive malignant neoplasia in the case of CINIII, CINII, CINI were 4%, 57.1%, and 37%, respectively. Sensitivity, specificity, and positive and negative predictive values for colposcopy in cervical intraepithelial neoplasia were reported as 57.3%, 51.8%, 23.3%, and 82.5%, respectively.

Conclusion: This study showed an acceptable correlation between colposcopic examination and histopathologic findings. Thus colposcopy can be used as a tool for early diagnosis of precancerous cervical lesions as a screening method alongside the pap smear. The correlation between the experience of examiner and accuracy of colposcopy results were not meaningful.

Keywords: Biopsy, Colposcopy, Correlation, Histopathology

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Introduction

According to the World Health Organization, Cervical cancer ranks as the fourth most frequently diagnosed cancer and the fourth leading cause of death from cancer in women. The GLOBOCAN 2018 estimates 570,000 cases and 311,000 deaths in 2018

worldwide with this disease. The incidence is considerably higher in developing countries, where more than 87% of cases can be found (1). Based on a report by the National Cancer Registry Center of Iran in 2013, the mean age-specific incidence rate of cervical cancer was 2.5 in 100,000 individuals (range: 0.4

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[Zanjan, Iran] - 4.1 [Fars, Iran]), and this cancer was the 2nd most common gynecological cancer among Iranian women (2, 3). It is now understood that persistent cervical infection with high-risk HPV genotypes is necessary for the development of cervical cancer and its immediate precursor lesion, cervical intraepithelial neoplasia (CIN). In most patients, it spontaneously regresses back but in some patients over a period of 10 to 20 years, it has the potential to convert into cervical cancer (4). Cervical intraepithelial neoplasia (CIN) often arises in an area of metaplasia in the transformation zone at the advancing squamocolumnar junction (5). Colposcopy is a worldwide accepted method for detection of early carcinoma of cervix, as it gives faster result and guides the site of biopsy which can be done in a single visit proving itself as a better screening modality for premalignant lesion. The diagnostic algorithm of various organized screening program consists of cytology and colposcopy, which helps in detecting the abnormality and can be established by histological grade of lesion (6, 7). Colposcopy is the visual inspection of the cervix under magnification, and is one of the first steps in the diagnostic workup of women with abnormal cervical cytology. For colposcopy to be deemed satisfactory, the squamocolumnar junction and the transformation zone must be visible. The criteria for positive colposcopy results are well established and include the detection of blood vessel abnormalities (punctuation, mosaic, and atypical vessels), whitening of the epithelium after the application of acetic acid, color changes after the application of iodine, changes in size, and demarcation (8-10). Most reports have shown a perfect agreement between the colposcopic impression and histology of only 32-37%, with the weighted kappa strength of agreement of only 0.20-0.26. The agreement of the colposcopic diagnosis and cervical pathology within one grade has been reported to be only 75% - 77%, and nearly one-third of high-grade squamous

intraepithelial lesions (HSIL) were under graded (11-13). Hence the aim of the present study was to determine the accuracy of colposcopic diagnosis in the patients with cervical lesions.

Materials & Methods

This study was a cross-sectional comparative study and was conducted in accordance with the approved guidelines with the ethical code of IR.UMSU.REC.1400.100 from the Ethics Committee of Urmia University of Medical Sciences (UUMS). The study was performed on 436 women with abnormal Pap smear test results referring to Motahari Hospital, Urmia during March 2021 to March 2022. The inclusion criteria for entering the study included healthy, non-pregnant women who were married, had abnormal Pap smear test results, and completed biopsy and colposcopy findings. Exclusion criteria included incomplete cases, women who have had previous medical, therapeutic interventions of the cervix (such as cryotherapy), and previous cervical surgery or cervical stenosis. The details of patient information collected as follows: Demographic data (age, level of education, smoking, parity), clinical findings (vaginal discharge, vaginal bleeding, post-coital bleeding, and spotting), Pap smear cytology (Inflammation: Mild, moderate, severe, ASCUS, ASC-H, Low-grade squamous intraepithelial lesion (LSIL), and High-grade squamous intraepithelial lesion (HSIL)), colposcopy findings (Acetowhite, abnormal vascular pattern (mosaism), and cervical ulcer), histopathology findings (Cervicitis, CIN I (LSIL), CIN II and CIN III (HSIL)), and examiner experience. All information was recorded on a checklist. In this study, the conventional Pap smear was used. Colposcopy and histopathologic findings of individuals with abnormal Pap smear results were extracted from the patient records. The data were analyzed using descriptive and analytic statistics (Chi-square test) using SPSS 21 (SPSS Inc., Chicago, IL., USA). The

sensitivity, specificity, positive and negative predictive values of various diagnostic methods were calculated ($P < 0.05$).

Results

In this study, 436 female patients who referred to the gynecology clinic of Urmia Motahari Hospital for

colposcopy were examined. The average age of the women under investigation was 37.3 ± 9.60 years old. The most common pathological findings in colposcopy examinations in order of frequency were Acetowhite lesions (AW), ulcers and erosions, polyps, genital warts, CIN I, CIN II, CIN III, cervical mass, and finally cervical cancer. (Table 1).

Table 1. Distribution of the study population according to the colposcopic appearance of cervix

DIAGNOSIS	No.	Percent
AW	156	35.80
POLYP	21	4.80
NORMAL	150	34.40
CIN I	25	5.70
CIN II	14	3.20
CIN III	8	1.80
WART	24	5.50
SCC	5	1.10
ULCER	19	4.40
INFLAMMATION	4	0.90
MASS	10	2.30
TOTAL	436	100

The most common pathological findings, in order of prevalence, were inflammation (acute, chronic and

ulcerative), metaplasia, normal, CIN I, CIN II, polyp, CIN III, invasive cancer, and genital wart (Table 2).

Table 2. Distribution of the study population according to histopathologic findings

HISTOPATHOLOGY RESULT	No.	Percent
INFLAMMATION	144	33
POLYP	20	4.60
NORMAL	70	16.10
CIN I	32	7.30
CIN II	24	5.50
CIN III	19	4.40
METAPLASIA	109	25
SCC	14	3.20
WART	4	0.90
TOTAL	436	100

The correlation between colposcopic and histopathologic findings were 79.2% in non-neoplastic lesions, 35.6% in benign neoplasia, 18.7% in non-

invasive malignant neoplasia, and 80% in invasive neoplasia. Also, the Kappa coefficient of agreement was calculated to be 0.06 (Table 3).

Table 3. Correlation between colposcopy and histopathology

colposcopy	histopathology	histopathology				total
		Non-neoplastic	Benign neoplasm	Non-invasive neoplasia	Invasive neoplasia	
Non-neoplastic	Number	137	3	33	0	173
	percent	79.20	1.7	19.1	0	100
Benign neoplasm	Number	24	16	4	1	45
	Percent	53.30	35.6	8.9	2.2	100
Non-invasive neoplasia	Number	162	2	38	1	203
	percent	79.8	1	18.7	0.5	100
Invasive neoplasia	Number	0	3	0	12	15
	percent	0	20	0	80	100
total	Number	323	24	75	14	436
	percent	74.1	5.5	17.2	3.2	100

According to the comparison, the agreement percentage of colposcopy and histopathology findings in noninvasive malignant neoplasia in the case of CINIII, CINII, and CINI were 4%, 57.1%, and 37%,

respectively. Sensitivity, specificity, positive and negative predictive values for colposcopy in cervical intraepithelial neoplasia were reported as 57.3%, 51.8%, 23.3%, and 82.5%, respectively.

Table 4. Sensitivity, specificity, PPV and NPV of colposcopy in cervical intraepithelial neoplasia

Sensitivity	57.303%	46.370% to 67.737%
Specificity	51.873%	46.475% to 57.239%
AUC	0.546	0.498 to 0.593
Positive Likelihood Ratio	1.191	0.965 to 1.469
Negative Likelihood Ratio	0.823	0.634 to 1.069
Disease prevalence	20.413%	16.727% to 24.506%
Positive Predictive Value	23.394%	19.843% to 27.365%
Negative Predictive Value	82.569%	78.486% to 86.015%
Accuracy	52.982%	48.175% to 57.747%
confidence interval:95%		

Among those with colposcopy result of invasive cervical neoplasia (SCC), 4 cases had SCC and 1 case had polyp in the histopathology report. Among the patients whose histopathology results were positive for SCC, 2 cases had colposcopy report based on wart, one case with CIN III, 8 cases with mass, and 4 cases with

SCC. Finally, according to the conducted investigations, the sensitivity, specificity, positive and negative predictive values for colposcopy in the case of invasive cervical neoplasia were reported as 61.9%, 47.6%, 27.6%, and 79.48%, respectively (Table 5).

Table 5. Sensitivity, specificity, PPV and NPV of colposcopy in invasive cervical carcinoma

Sensitivity	61.905%	45.637% to 76.428%
Specificity	47.692%	38.863% to 56.629%
AUC	0.548	0.470 to 0.624
Positive Likelihood Ratio	1.183	0.887 to 1.579
Negative Likelihood Ratio	0.799	0.522 to 1.222
Disease prevalence	24.419%	18.201% to 31.540%
Positive Predictive Value	27.660%	22.272% to 33.784%
Negative Predictive Value	79.487%	71.688% to 85.570%
Accuracy	51.163%	43.439% to 58.846%
confidence interval:95%		

The agreement percentage of colposcopy and histopathological findings in examiner 1 with more experience in benign and malignant lesions were 47.7% and 61.9%, respectively, and in examiner 2 with less experience in benign and malignant lesions were 54.4%

and 54.3%, respectively. Kappa coefficient for correlation between colposcopy and histopathology results was calculated by examiner 1 with more experience as 0.068 and by examiner 2 with less experience as 0.042 (Table 6).

Table 6. Correlation between colposcopy and histopathology according to experience of examiner

		colposcopy	histopathology		
			benign	malignant	total
Examiner1	benign	No.	62	68	130
		percent	47.7	52.3	100
	malignant	No.	16	26	42
		percent	38.1	61.9	100
Examiner2	benign	No	118	99	217
		Percent	54.4	45.6	100
	malignant	No.	22	25	47
		Percent	46.8	53.2	100
Total	No.	140	124	264	
	Percent	53	47	100	

Discussion

Cervical cancer is the second most frequent cancer worldwide in women after breast carcinoma. However, invasive cancer of the cervix is considered to be a preventable condition as it is associated with a long pre-invasive stage (CIN), making it amenable to screening and treatment (14). An effective screening program can lead to earlier detection of cancer and its precursor lesions, thus leading to a decline in mortality. Colposcopy is a good diagnostic tool for evaluation of premalignant conditions of the cervix correlates well with histopathological findings (15, 16). However, the colposcopic accuracy has always been questioned because agreement between colposcopic diagnosis and cervical biopsy analysis varies between countries and even between hospitals (17). We reviewed the colposcopic and histopathologic results of 436 women who came to the hospital with various symptoms and unhealthy cervix and belonged to a high-risk group. The colposcopic diagnosis of CIN requires an understanding and recognition of four main features: color tone, intensity of acetowhitening, margins and surface contour of acetowhite area, vascular pattern, and iodine staining. Variations in quality and quantity of these atypical appearances help in differentiating CIN from other lesions and between grades of CIN (18). The mean age of women in our study was 37 years. This corresponds to 34.5, 36, and 36 in studies done by Pandey et al., Goel et al., and Durdi G et al. respectively (19-21). In our study, 150 (34/4%) out of 436 patients showed normal and 286 (65/5%) showed abnormal colposcopic findings. In our study, the most common finding was acetowhite lesions (35%) in colposcopy and chronic cervicitis (33%) in histopathological findings. This was similar to the results of the study by swati et al. the most common colposcopic finding was acetowhite lesions (48%) and chronic cervicitis (45%) in histopathological findings (22). In this study, histopathology confirmed chronic cervicitis in 144

(33%), 32 (7/3%) women with CIN I, 24 (5/5%) with CIN II, and 19 (4/3%) with CIN III. Correlation between colposcopic findings and histopathological findings in intraepithelial neoplasia was 36.17% that is lower than these two studies: In a study by Patil et al. (16), which colposcopy was done in 120 women with cervical erosion. Histopathology findings correlated in 44 (88%) women and did not correlate in 6 (12%) women, and in a study by Boicea et al. (23), which the correlation was 78.5% in the CIN I category, 84% in the CIN II category, 88.6% (133 out of 150 patients) in the CIN III category, 46.1% for micro invasive carcinoma, and 50% for CIS. On the other hand, the exact correlation between colposcopy and histopathology in CIN I was very low (most cases of CIN I in histopathology were underestimated in colposcopy). In a study by GS Durdi et al. (21) 67.1% of CIN I cases were estimated accurately in colposcopy. It should be noted that differences may be due to the use of colposcopic terminology, as well as heterogeneous sample characteristics, and the level and experience of colposcopists (17).

In our study, sensitivity and specificity for colposcopy in cervical intraepithelial neoplasia were reported as 57.3% and 51.8%, respectively. Sensitivity and specificity of colposcopy were comparable with other studies mentioned as follows: study of Anying Bai (17) with sensitivity of 42.35% and specificity of 77.6%, study of Savitha (24) with sensitivity of 85% and specificity of 83.5%, and study of Samiee Rad (25) with sensitivity of 74.7% and specificity of 39.5%.

Compared with similar studies, the sensitivity, specificity, and positive predictive value of colposcopy in this study was equivalent to other studies, and its sensitivity and specificity were within the modest range of other studies. The sensitivity of this method varied from 45% to 97% and its specificity varied from 19% to 90% in different studies (26, 27)

The results of this study also showed that the percentage of agreement between colposcopy and histopathology findings for the examiners with more and less experience was not statistically significant. Many studies have aimed to compare the accuracy and differences between colposcopic evaluators. In a study by Ples et al. (28) with two colposcopic evaluators (one in vivo and one by computer-saved images), there was no significant difference between the two, but in a study by Bifulco G et al. (29) the high correlation was lost when colposcopy was performed by less experienced examiner (junior group). On the other hand, in the senior group exact agreement was found in 85.1 % of grade 1 lesions and in 51.5 % of grade 2 lesions. In another study by Vallikad et al. the inter-observer agreement for the TZ type classification was moderate ($Kappa= 0.53$ to 0.66), and the Intra-observer agreement was moderate to strong (0.60 to 0.86)(30).

Conclusion

Our results suggest that colposcopy has the acceptable diagnostic accuracy in comparison with histopathology in high-grade lesions but the exact correlation in low-grade intraepithelial neoplasia is low. So due to the efficacy of colposcopy along the pap smear, Hpv typing, and histopathology, and by considering the limitations in the health system to provide the HPV genotyping test, the importance of all these three tests should be considered.

The main limitation of this study was its retrospective nature and the restrictions on HPV evaluation. However, large sample size and conducting the study at an Obstetrics and Gynecology Academic Hospital with patients from lower or middle society classes was the strength of this study. Long-term prospective studies along with pap smear and HPV genotyping test are recommended in order to improve the national guidelines in various regions. On the other hand, colposcopy using RCI which was not used in this

study is recommended due to satisfactory diagnostic efficacy and the good correlation between colposcopic impression and histopathology.

Acknowledgements

We announce our special thanks to the gynecology and pathology departments staff of Shahid Motahari Hospital for assisting us in this project.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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