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The Values of Colposcopy in Patients with the Diagnosis of the High-Grade Squamous Intraepithelial Lesion in Routine Papanicolaou Test

Tajossadat Allameh, Maryam Kalatehjari*

Department of Obstetrics and Gynecology, Isfahan University of Medical Sciences, Isfahan, Iran

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Corresponding Information:
Maryam Kalatehjari,
Department of Obstetrics and Gynecology, Isfahan University of Medical Sciences, Isfahan, Iran
Email: mk.medicine@yahoo.com

ABSTRACT

Background & Objective: Cervical cancer is one of the most preventable malignancies that can also be diagnosed in the early stages through screening tests. The Papanicolaou test (Pap smear) is the most conventional means for screening, while studies represent acceptable and more accurate outcomes of colposcopy in contrast to Pap smear. The current study aims to assess the values of colposcopy for cervical cancer diagnosis.

Materials & Methods: This is a cross-sectional study conducted on 94 patients diagnosed with high-grade squamous intraepithelial lesion (HSIL). After that, colposcopy was performed for all patients, and findings were presented as normal, chronic cervicitis, the thin acetowhite lesion (AWL), dense/thick AWL, AVP, pilling, and cauliflower-like mass. The biopsies were taken and pathological studies, as the gold standard was interpreted as normal, cervicitis, atypical squamous cells of undetermined significance (ASCUS), cervical intraepithelial neoplasia-1, -2 or -3 (CIN-1, -2 or -3), carcinoma-in-situ (CIS), adenocarcinoma and invasive squamous cell carcinoma (SCC).

Results: The pap-smear results were significantly associated with the biopsy reports (P<0.001; kappa=0.225). Besides, significant concordance was found between colposcopy and biopsy (P<0.001; kappa=0.247). The total sensitivity and specificity of colposcopy were based on the biopsy findings as the gold standard was 97% and 41%, respectively (P<0.001).

Conclusion: Colposcopy was significantly sensitive and specific for diagnosing both non-malignant CIN-1 and malignant cervical lesions, but not for CIN-2, -3, and CIS lesions. Further evaluations are strongly recommended.

Keywords: Cervical intraepithelial neoplasia, Colposcopy, Papanicolaou test, Sensitivity and specificity

Introduction

Cervical cancer is the second most common cancer of females worldwide that affects 530000 new cases annually and causes death in over 270000 females each year **(1)**. This malignancy is remarkable for developing countries as about 80% of the deaths due to cervical cancer are reported in these countries **(2)**.

On the other hand, this cancer is one of the most preventable ones that can be diagnosed in early curable stages. The Papanicolaou test (Pap smear) is the most cost-effective and conventional means for screening and probably early cervical cancer diagnosis **(3)**. In cases presenting abnormal pop smear, colposcopy and endocervical curettage or biopsy may be required to confirm the diagnosis **(4, 5)**.

Considering the remarkable high rate of heterogenicity in the Pap smear capability of correct diagnosis with the high rate of false-negative reports in up to 49% of the cases, there is no unified about the most efficient means for the most accurate early diagnosis of cervical cancer **(5)**.

Although limited studies are presenting acceptable and more accurate outcomes of colposcopy in contrast to Pap smear, their supporting data are still conflicting as there are studies showing discordance of colposcopy findings with the definite histological diagnosis through biopsy **(6-9)**.

In the current study, we have aimed to assess colposcopy values in contrast to the histological findings of the cervix biopsies among females with Pap smears suspected for cervical cancer.

Material and Methods

The current report is a cross-sectional study conducted on 94 patients diagnosed with the high-grade squamous intraepithelial lesion (HSIL) in Pap smear referred to Shahid-Beheshti Hospital affiliated at Isfahan University of Medical Sciences, Iran, from December 2016 to December 2018.

All patients diagnosed with HSIL based on the findings of Pap smear who have undergone both colposcopy and histological study through biopsy were included. Those who presented their unwillingness to participate in the study and patients who had impaired records of either colposcopy or histology were excluded.

The Ethics Committee of Isfahan University of Medical Sciences approved the study protocol (ethical code: IR.MUI.MED.REC.1397.312). After that, all of the study-associated required information was provided to the study participants, and they were reassured about the confidentiality of their data. The participants were requested to sign a written form of participation in this study.

The patients were initially examined macroscopically by vaginal examination. Also, a conventional Pap smear test was performed for all patients 8 weeks after the first Pap smear. The Bethesda scale was the basis for interpreting the samples. Based on the diagnosis of HSIL in the Pap smear, the colposcopy was performed for the patients by a skilled target gynecologist. The colposcopies were done using either acetic acid 5% or iodine solution 12%. The transitional squamous, columnar zone detection was considered the satisfactory colposcopy **(10)**. The presence of acetowhite lesions with vascular and/or epithelial lesions was considered as positive colposcopy. The colposcopic findings were normal, with chronic cervicitis, the thin acetowhite lesion (AWL), dense/thick AWL, AVP, pilling, and cauliflower-like mass.

Biopsies were taken from all patients and interpreted by a target skilled pathologist to minimize the potential inter-observer bias. The biopsies were presented as normal, cervicitis, atypical squamous cells of undetermined significance (ASCUS), cervical intraepithelial neoplasia-1, -2 or -3 (CIN-1, -2 or -3), carcinoma-in-situ (CIS), adenocarcinoma and invasive squamous cell carcinoma (SCC). The results of the biopsies were regarded as the gold standard, and then the colposcopy findings were compared accordingly. Besides, the findings of conventional Pap-smear were compared with biopsy as well. Human papillomavirus (HPV) was not assessed through laboratory tests, and only the pathologic changes contributed to the HPV contamination found through biopsies were reported as the HPV positivity.

The obtained data were entered into the SPSS (SPSS Inc., Chicago, IL., USA) version 20 and analyzed. The descriptive data were presented in mean and percentages. ROC curves and the area under the curve (AUC) were measured for analytics. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were measured. A P-value of less than 0.05 was considered as a significant level.

Results

The study population had a mean age of 41.67±11.42 years (range: 21-81 years) and a mean age of 20.04±4.21 years at the marriage time (range: 13-35 years). The mean number of giving birth was 2.72±1.99 (range: 0-8).

Among the study population, sixty-seven (71.2%) of the patients did not use contraceptives. Further information about the type of contraception is presented in Table 1. Thirty-seven (39.4%) of the patients required no further intervention while 22 (23.4%) underwent conization biopsy; among them, eight (8.51%) required a transabdominal hysterectomy, and five (5.31%) with the worst biopsy reports underwent a radical hysterectomy.

Table 1. Demographic information of the study population

Variable		
Age (mean± SD)		41.67±11.42
Age at marriage (mean± SD)		20.04±4.21
Number of giving birth (mean± SD)		2.72±1.99
Contraception (%)	Nothing	67 (71.2%)
	Withdrawal	6 (6.4%)
	Oral contraceptive	5 (5.3%)
	Tube ligation	7 (7.4%)
	Barrier	6 (6.4%)
	Vasectomy	3 (3.2%)

Biopsy findings were normal, LSIL (CIN 1, 2), HSIL (CIN 3 or CIS) and invasive carcinoma in 51 (54.2%), 16 (17.02%), 22 (23.4%) and 5 (5.3%) cases respectively. Based on Table2, the pap-smear results were significantly in accordance with the biopsy reports (P<0.001). Based on Table 2, the kappa coefficient index was 0.225.

The findings, including normal, thin AWL, thick AWL, and AVP/pilling/cauliflower lesions, were found in 22 (23.4%), 38 (40.42%), 26 (27.65%), and 8 (8.51%) colposcopies, respectively. Table 2 represents biopsy and colposcopy results in detail. Based on Table 2, significant concordance was found between colposcopy and biopsy with a P-value of <0.001 and a kappa coefficient index of 0.247.

Table 2. Kappa coefficient assessments based on pap-smear*biopsy, colposcopy*biopsy

		Pap-smear				Total
		Normal	LSIL/ ASCUS	HSIL	Invasive carcinoma	
Biopsy	Normal	42	1	8	0	51
	LSIL	6	2	7	1	16
	HSIL	9	5	8	0	22
	Invasive carcinoma	1	1	2	1	5
		58	9	25	2	94
		Colposcopy				
		Normal	Thin AWL	Thick AWL	AVP/pilling + caul-flower lesion	Total
Biopsy	Normal	21	21	5	4	51
	LSIL	0	7	7	4	16
	HSIL	1	9	12	0	22
	Invasive carcinoma	0	1	2	2	5
		22	38	26	8	94
		Normal		Abnormal		
Biopsy	Normal	21		30		51
	Abnormal	1		42		43
	Total	22		72		94

Based on the findings above, the colposcopy could statistically diagnose normal, CIN-1 and invasive SCC/adenocarcinoma/AVP/cauliflower lesion and pilling cases (P<0.05) but was not significantly in association with the correct diagnosis of CIN-2, -3 and CIS (P>0.79). Based on Table 3, the sensitivity and specificity of colposcopy for the diagnosis of normal cases were 82% and 60%, for CIN-1 were 56% and 68% and for invasive SCC/adenocarcinoma/AVP/-cauliflower lesion and pilling (cancerous lesions) were 80% and 66%, respectively. Based on the last part of Table 3, colposcopy's total sensitivity and specificity based on the biopsy findings as the gold standard were 97% and 41%, respectively. This assessment revealed a statistically significant association (P<0.001) with a kappa index of 0.369.

Table 3. Sensitivity, specificity, positive/negative likelihood ratio and area under curve based on the diagnoses of colposcopy

	Index	Colposcopy
Normal &/or cervicitis	Sensitivity	82%
	Specificity	60%
	Positive likelihood ratio	2.05

	Index	Colposcopy
CIN-1 (Thin AWL)	Negative likelihood ratio	0.3
	AUC (CI 95%)	0.764
	P-value	<0.001
	Sensitivity	56%
	Specificity	68%
	Positive likelihood ratio	1.75
	Negative likelihood ratio	0.64
CIN-2 & -3 & CIS (Thick AWL)	AUC (CI 95%)	0.676
	P-value	0.028
	Sensitivity	57%
	Specificity	69%
	Positive likelihood ratio	1.83
	Negative likelihood ratio	0.62
Invasive SCC or adenocarcinoma, AVP cauliflower lesion & pilling	AUC (CI 95%)	0.643
	P-value	0.761
	Sensitivity	80%
	Specificity	66%
	Positive likelihood ratio	2.35
	Negative likelihood ratio	0.30
Total values for colposcopy	AUC (CI 95%)	0.793
	P-value	0.028
	Sensitivity	97%
	Specificity	41%
	Positive predictive value	58%
	Negative predictive value	95%
	P-value	<0.001

Discussion

The required time for the progression of precancerous lesions of the cervix to the incurable malignant masses can clarify the necessity of using an appropriate means with the highest accuracy to make an on-time definite diagnosis **(11)**.

Studies in the literature have shown that Pap smear as the most popular screening test is not reliable enough to make the diagnosis and further therapeutic approaches **(12, 13)**. In the current study, we observed the remarkable concordance of Pap-smear with the biopsy reports (P<0.001, kappa=0.225). Contrary to our study, Lonky *et al*. conducted a study presenting a low non-significant correlation of Pap-smear with cytology findings presenting high-grade dysplasia, while it had higher sensitivity and specificity for the correct diagnosis of malignant lesions **(14)**. Other studies represented better outcomes of Pap-smear with the sensitivity of 34-57% and specificity of 85-97% for the correct diagnosis of high-grade intraepithelial lesions and malignant ones. In general, studies are unanimous about the ability of Pap-smear for the correct diagnosis of malignant lesions. However, the

matter is about the early diagnosis to prevent progressed masses **(15, 16)**. We think the high specificity presented by mentioned studies is mostly attributed to detecting malignant lesions but LSIL or HSIL. Surprisingly, a study in China presented a high sensitivity rate of 85%, again for detecting non-benign lesions; malignant ones are included **(17)**.

This study tried to assess the accuracy of colposcopy for the correct diagnosis of cervical lesions based on biopsy as the gold standard. Our findings represented that colposcopy was in statistical concordance with the findings obtained from biopsies (P<0.001; kappa-=0.247). Furthermore, a remarkable association was found for the correct diagnosis of normal, CIN-1, and cancerous lesions. The highest sensitivity was detected for normal/cervicitis diagnosis (82%), followed by cancerous lesions (80%) and then CIN-1 (56%). Hence, the most significant specificity was found for CIN-1 (68%), followed by lesions representing cancer (66%) and normal/cervicitis (60%). In general, the colposcopy study of the cervix represented the notable sensitivity of 97% and specificity of 41%.

Colposcopy for the early diagnosis of cervical lesions has been assessed for a long time in the literature, but the reports are confusingly controversial. An old study by Maiman *et al.* presented inferior findings than ours, reporting the sensitivity and specificity of 80% and 29% in general. It was 83% and 27% respectively for high-grade lesions **(18)**.

A pilot study by McAdam *et al.* on 496 females declared the specificity of 77% and sensitivity of 99% for colposcopy assessments of CIN-2 or worse conditions **(19)**. We have not found the remarkable capability of colposcopy for the proper early diagnosis of CIN-2, -3, and CIS lesions.

The other study by Sayyah-Melli was conducted on 315 patients. Similar to this study, they considered histological findings as the gold standard and presented sensitivity and specificity of 90.3% and 90.9%, respectively **(20)**. Their outcomes regarding colposcopy ability in the correct diagnosis of cervical lesions were surprisingly higher than ours.

The other study performed by Karimi *et al.* in Yazd presented 80% of both sensitivity and specificity for colposcopy for the early diagnosis of precancerous lesions in the cervix **(21)**.

Karimi-Zarchi *et al.* designed their study to compare colposcopy with other Pap smear and cytology techniques. They eventually presented 70.9% of sensitivity and 44.4% of specificity for colposcopy. Similar to this study, they presented a statistical association of colposcopy with cytology findings **(11)**.

Remarkable differences in the studies about the ability of colposcopy in the correct detection of non-benign cervical lesions may be attributed to the operator skill, quality of colposcopy performance and interpretation, and the classification of the lesions.

Other studies in this term have unanimously presented the superiority of colposcopy over Pap smear while the values of this technique for correct diagnosis were diverse **(3, 22, 23)**. In this term, further studies are recommended.

Conclusion

Based on this study, colposcopy findings were remarkably in concordance with histological reports. Furthermore, the colposcopic interpretations were significantly sensitive and specific for diagnosing both non-malignant CIN-1 and malignant cervical lesions. On the other hand, colposcopy assessments could not statistically diagnose CIN-2, -3, and CIS lesions correctly based on histological reports showing a notable limitation in diagnosing precancerous HISL. Further evaluations are strongly recommended.

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Conflict of Interest

The authors declared no conflicts of interest.

Statement of Ethics

The patient had signed the informed consent to report the present article.

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