

Colposcopy in Comparison with HPV-Pap Test for the Diagnosis of Cervical Intraepithelial Neoplasia 2

Maliheh Arab ^{1*}, Atefeh Moridi ¹, Maryam Maktabi ³, Nazanin Safaei ³, Behnaz Ghavami ³, Mahdie Sanati ⁴

¹ Imam Hossein Medical Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

² Department of Obstetrics and Gynecology, Arak University of Medical Sciences, Arak, Iran

³ Department of Obstetrics and Gynecology, Tehran University of Medical Sciences, Tehran, Iran

⁴ Developmental Biology, Science and Research University of Tehran, Tehran, Iran

* **Corresponding Author:** Maliheh Arab, MD, Ph.D, Imam Hossein Medical Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Fax: +98-2177543634, E-mail: drmarab@sbm.ac.ir

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Abstract

Introduction: The effectiveness of cervical cancer screening programs is an issue of concern in developing countries. It is a goal of researchers to find another solution or screening method to solve this problem. The current study aimed to compare the cost-effectiveness of the colposcopy and HPV-Pap test approaches.

Methods: This cross-sectional study examined 1944 asymptomatic women aged 30-70 years who had undergone colposcopy from 2013-2015. The cost of finding each CIN₂ case was obtained and compared with the cost of the HPV-Pap test finding.

Results: A pathology of CIN₂ or greater cases were reported in 43 cases (2.2%). The cost of finding each case by colposcopy was 2,456 USD and by PCR-Pap was 2,966 USD ($P < 0.0001$).

Conclusion: The cost of finding each CIN₂ or greater case by HPV-Pap test was 1.32 times that of a colposcopy. Colposcopy in this setting was more cost-effective and should be considered in similar settings.

Keywords: Colposcopy, HPV-Pap Test, CIN₂; Iran, Cost-effectiveness

Introduction

In many Western and developed countries, including the United States (US), cervical cancer is the third-most-common form of cancer. It ranks third in the cause of cancer mortality among gynecologic cancer patients after endometrial and ovarian cancer.^{1,2} In regions of the world where cervical cancer screening is not appropriately managed, it is the second-most-common form of cancer among female cancer patients (17.8 per 100,000 women) and has a cancer mortality rate of 9.8 per 100,000.^{1,2}

Screening programs for the diagnosis and treatment of precancerous and early-stage cancer in patients have reduced cervical cancer incidence and mortality.³⁻⁶ The suggested age of screening in the US is 21 years if asymptomatic, without immunodeficiency and with a history of sexual activity.⁷ In other countries, screening begins at 20-25 years of age.⁸ A panel considering the most up-to-date evidence recommended screening for those under the age of 30 years by Pap alone at 3-year intervals and for those over the age of 30 years at 3-year intervals by Pap as a

co-test with HPV testing (HPV-Pap) and at 5-year intervals if both remain negative. For women over the age of 65 years with a regular history of screening and negative results, the harm-benefit of screening favors no screening. The US Preventive Services Task Force suggests screening to the age of 70 to 75 years.⁹

Undoubtedly, the decrease in the incidence and mortality rate of cervical cancer in most Western and developed countries is due to well-managed and systematic Pap testing.¹⁰⁻¹³ For instance, appropriate and systematic screening in Nordic countries has resulted in an 80% reduction in cervical cancer incidence.¹³⁻¹⁶ Unfortunately, these appropriate and systematic screening plans resulting in an epidemiological change in cervical cancer rates are not implemented in most developing countries.^{11,13-16} This practical point has guided researchers to find another solution.^{10-14,16}

Many other screening methods have been suggested besides the Pap test which include the Visual Inspection with Acetic acid (VIA) or Lugol (VIL1), Cervicography, Speculoscopy, Colposcopy, and

liquid-based automated cytology, all considered for special backgrounds.^{11-13,15-17} These screening methods increase the cost of colposcopy because a specialist and specialized facilities are required, which is what deters the use of colposcopy as a first step. In this study, the cost-effectiveness of colposcopy as the first step for the diagnosis of CIN₂ or greater cases was evaluated.

Materials and Methods

In this cross-sectional prospective study, all married women aged 30-70 years who referred for routine screening to the charity center of a tertiary subspecialty medical center located in Tehran from 2013 to 2015 were included in the study. All the women were tested by colposcopy screening. Women who had been hysterectomized were pregnant, those previously diagnosed with cervical neoplasia and those who exhibited physical-mental disorders (were unable to cooperate) were excluded. The remaining 1944 cases were included in the study after demographic data were recorded.

All colposcopies performed by one expert Gynecologist using one-colposcopy instrument (D.F. Vasconcellos; Brazil). The colposcopies were performed under $\times 10-40$ magnification using white and green lighting before and after use of 3% acetic acid. Lugol was not used in this study.

The colposcopy report sheets were ranked as satisfactory, leukoplakia, acetowhite region, punctuation, mosaicism or atypical vessels. In the case of an abnormal colposcopy, sampling was done and, after fixation in formalin (10%), the sample was sent to the common pathology laboratory of the university. Two pathologists in the same laboratory, both with more than 10 years of experience, reviewed the samples.

The gold standard for case finding (CIN₂ or greater) was biopsy under colposcopy. The cost of finding a case by biopsy-colposcopy in the present study was compared with the expected cost of HPV/Pap test, which was estimated using the end result of a similar

population for the prevalence of finding CIN₂ or greater cases. Statistical analysis was done in SSPS v. 17.0 (SPSS; USA). A p-value of less than 0.05 was considered statistically significant.

Estimation of Cost

The cost of the procedures was estimated at the time of manuscript preparation for all cases regardless of the true cost at the time of performance. The cost was calculated based on the set of government payment. The cost of an HPV test is equal in governmental and private settings. An exchange rate for the Iranian Rial (IRR) to USD was done for a better understanding of the findings.

Ethical Considerations

The study followed the principles of the Helsinki Declaration and was approved by the Medical Ethics Review Board of Shahid Beheshti University of Medical Sciences. All information about the women was kept fully confidential and all information was released as a group without the use of participant names. The participants incurred no costs and the study protocol did not harm the participants. Written informed consent was obtained from the participants and the details and purpose of the study were disclosed to them.

Results

The colposcopy-screening group comprised 1944 cases with a mean age of 46.8 ± 8.8 years and a median age of 46 years. Colposcopy and pathologic reports of patients are shown in Table 1.

The Pap smear reports were reviewed at the same time that the colposcopy reports were reviewed. An abnormal Pap smear was reported in less than 1% of cases. The cost of each finding of CIN₂ or greater by colposcopy was 51 USD (1989 colposcopy-biopsy cases) and 19 USD (46 colposcopy cases). The total cost of every finding of CIN₂ or greater was 2,473 USD (Table 2).

Table 1. Colposcopy and Pathologic Findings of Colposcopy Screening

	Satisfactory	Unsatisfactory	Total	High colposcopy score**	Low colposcopy score	Total	CIN2 or more	Less than CIN2 total 1944(100)
Total screening group N (%)*	530 (27.3)	1414 (72.7)	1944 (100)	1019 (52.4)	925 (47.6)	1944 (100)	43 (2.2)	1901 (97.8)
CIN₂ or more cases N (%)*	9 (20.9)	34 (79.1)	43 (100)	32 (74.4)	11 (25.6)	43 (100)	-	-

Table 2. Calculation Chart of Finding Each Case of CIN₂ or More

Procedure	Cost
Cost of each Colposcopy-biopsy	51 USD
Number of colposcopy-biopsies	1898
Total Cost of colposcopy-biopsies	96798 USD
Cost of each Colposcopy	19 USD
Number of colposcopies	46
Total Cost of colposcopies	874 USD
Total cost of all procedures	97672 USD
Each case finding cost	2273 USD

Discussion

In the present study, among the 43 CIN₂ or greater cases were found. Thirty-two out of 43(74.4%) were high score and 11(25.6%) were a low score in colposcopy. Low-score colposcopic findings were considered less effective predictors of CIN₂ or greater case findings and could guide the colposcopist to be more conservative about the biopsy of normal tissue, resulting in decreased costs. If the biopsy under colposcopy is done only for high-score colposcopy cases, the total cost would be 69,696 USD or 1,621 USD for each case. Under such conditions, our study revealed that 11 (25.6%) cases could have been missed. In future studies, the determination of strong predictors identified by colposcopy for finding CIN₂ or greater cases could reduce the number of biopsies and the costs. In the present study, dense acetowhite, peeling, punctuation, mosaicism, atypical vessels and large lesions in colposcopy were regarded as high-score items.

Syrjänen et al. examined 3437 cases in Buenos Aires who had undergone Pap tests, HPV tests and colposcopy at the same time. Positive Pap and HPV results were reported to be 4% and 16.9%, respectively. Colposcopy in this screening method was indicated for an abnormal Pap test or positive HPV test. Abnormal colposcopy results were seen in 1189 (34.6%) cases and significant abnormal colposcopy were observed in 639 (18.6%) cases. A biopsy under colposcopy was done in 789 cases. A pathology of CIN₂ or greater were reported in 77 cases (2.2%) (13).

The cost of HPV/P/S co-testing in the Syrjänen et al. population was compared with that of colposcopy screening in the current study. The data from Buenos Aires revealed outcomes similar to the CIN₂ and greater outcomes in the present study: 43 out of 1944 (2.2%) in the current study and 77 out of 3437 (2.2%)

in Buenos Aires. The prevalence of positive HPV results in the Syrjänen et al. population was expected to be equal to that of the current study with an equal CIN₂ and greater frequency; thus, it was used for cost estimation (13).

If the population of the current study were screened by HPV/P/S, about 16.9% positive HPV and 4% positive Pap test results would be found. If CIN₂ or greater was used with the co-test method, colposcopy would be needed in 16.9% of cases with positive HPV and 4% with abnormal Pap smears. For the abnormal colposcopy findings (18.6%), biopsies were carried out. The expected cost of finding each CIN₂ or greater in a population similar to the population of the present study (Buenos Aires) when screened by the co-test method, would be as follows:

1. Cost of each Pap test: 10 USD
2. Number of pap tests: 1944
3. The total cost of Pap tests: 19.440 USD
4. Cost of each HPV PCR test: 47 USD
5. Number of HPV PCR tests: 1944
6. The total cost of HPV PCR tests: 91.368 USD
7. Cost of each colposcopy-biopsy: 47 USD
8. Number of colposcopy-biopsies: 361.6 (%18.6)
9. The total cost of colposcopy-biopsies: 18.451 USD
10. The total cost of all procedures: 136.247 USD (43 case findings)
11. Cost of each case finding: 2.976 USD

The cost of the HPV/Pap test method was higher in comparison with the colposcopy approach. The Pap test in the study population produced less than 1% positive findings. In this setting, with low Pap test accuracy, lower colposcopy cost in comparison with HPV-Pap and greater availability of colposcopy, it should be considered as a screening method. Further studies in the future should focus on decreasing the

need for biopsies in colposcopy cases by identifying the strong predictors of CIN₂ or greater case findings by colposcopy. A decrease in unnecessary biopsies would further reduce the cost of each CIN₂ or greater case finding by colposcopy.

In the present study, the total CIN₂ or greater case findings by colposcopy charged 2456 USD. The total cost of CIN₂ or greater case findings by PCR-Pap in a similar population was 2966 USD. There were significant differences between the two methods ($P < 0.0001$). The cost ratio of each case finding by HPV-Pap test in comparison with colposcopy and Pap test accuracy in that setting should be considered when selecting a method for mass screening in a specific society.

Conclusion

In the present study, the cost ratio of each CIN₂ or greater case finding by HPV-Pap test was 1.32 times that of the colposcopy approach. In this setting and other situations with a lower cost of colposcopy in comparison to HPV-Pap test and low quality of Pap test results, the colposcopy screening method might be considered as the preferred approach. There were some limitations to the present study. First, the Pap tests were performed in a setting with weak quality control. In addition, an expert Colposcopist in a research setting, which could result in bias, did the Colposcopies.

Authors' Contributions

MA and AM: Idea, data collection, critical appraisal and approval of the final content. NS, BG and MS: Data analysis and interpretation, results write up. MA, AM, MS, NS and BG: Data collection, manuscript write up, critical appraisal and approval of the final content.

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Conflict of Interest

The authors declare that they have no conflicts interest.

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