

Comparing the results of Pap smear and Direct Visual Inspection (DVI) with 5% acetic acid in cervical cancer screening

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ABSTRACT

Background: Cervical cancer is the most second common cancer among Iranian women. This study was carried out to compare the results of Pap smear method and Direct Visual Inspection (DVI) with 5% acetic acid in cervical cancer screening in Tabriz, Iran. **Material and Methods:** This cross-sectional study was carried out in Alzahra Therapeutic-Educational Centre, Tabriz, Iran in 2013 on 1000 women. First, Pap smear was done for all women, and then the cervix exposed with 5% acetic acid by cotton swab for 30 seconds and observed under adequate light. At the end, women with abnormal results in Pap smear or DVI method were referred to colposcopy and biopsy. Test's sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), LR+, LR- and confidence interval (CI) were determined ($P < 0.05$). **Results:** Nine-hundred and seventy-four (94.7%) cases were normal and had no abnormal findings and 26 (2.6%) participants had positive results in Pap smear or DVI test. Twelve women had abnormal Pap smear (nine women with atypical squamous cells of undetermined significance, ASCUS, three women with dysplasia, atypical endocervical, and low-grade squamous intraepithelial lesion, LSIL results) and 14 women had positive DVI (four women with human papillomavirus, HPV or koilocyte,) and one woman with abnormality in both method had carcinoma in biopsy that referred to oncologist. In this study the sensitivity, specificity, PPV and NPV for DVI were 71.4%, 50%, 35.7%, and 81.8% respectively in comparison with 14.3%, 50%, 10%, and 60% for Pap smear. **Conclusion:** As the DVI method has higher sensitivity and positive predictive value than Pap smear, it could be used as a useful method beside the Pap smear.

Key words: Cervical cancer, direct visual inspection, Pap smear

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INTRODUCTION

Cervical cancer is the second most common cancer among Iranian women.¹ 78% of cervical cancer happens in developing countries.^{2,3} The incidence of cervical cancer in East Azerbaijan of Iran, in 2003-2004 was 5.11 in 100000, while it was 11.9 in 100000 for high grade and 3.68 in 100000 for low grade pre-cancerous lesions.⁴ About half a million cases of invasive cervical cancer are diagnosed annually.^{5,6} The risk factors for cervical cancer

are: beginning sexual intercourse at early age, multiple sexual partners, history of HPV infection and genital wart in women and her partners, smoking, immune deficiency, multiparity, repetitive sexual transmitted disease, herpes simplex virus (HSV2), exposure of uterus to diethylstilbestrol (DES), history of intraepithelial lesion, familial history of cervical cancer, partner with penis cancer, cervical cancer in other partners of husband, low hygiene condition, and using oral contraception for a long time.^{4,7-9} Cervical cancer has a long pre-invasive period, so it is preventable.¹⁰ Dysplasia usually has no clinical sign and its diagnosis is often made based on cytological findings using the Pap smear test.⁸

According to Agency for Healthcare Research and Quality (AHRQ), the sensitivity of conventional cytology testing in detecting precancerous lesions was 51% and for diagnosis of cervical intraepithelial neoplasia grade 1, (CIN1), 2 was 47-62% and its specificity was 59-60%.⁹ About 30% of new

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cases of cervical cancer, each year, occur in women that had Pap smear but due to errors in sampling, fixation, and interpretation, it has been incorrectly reported as normal, moreover in developing countries there is often lack of necessary resources to use Pap smear as a screening tool for cervical abnormalities.⁸

Because the burden of cervical cancer is high, the alternative techniques have been sought. Recently, interest in Direct Visual Inspection with acetic acid (DVI) has been increased. DVI method doesn't need laboratory facilities and its result is identify in the same visit, so this causes save the cost and time of patients.⁸ Numerous studies have been conducted on its sensitivity and specificity to detect cervical lesions when compared with other techniques in which its sensitivity ranged between 66-96% and specificity between 64-98%.¹¹

The studies suggest that DVI could be a primary screening tool, with low biopsy rate especially in low-resource settings or where cytological testing services are suboptimal.¹²

This study was conducted to compare the results of Pap smear and DVI method in diagnosis of cervical premalignant lesions.

MATERIALS AND METHODS

This cross-sectional study was carried out in Alzahra Therapeutic Educational Centre, Tabriz, Iran in 2013 on 1000 women. Sample size using Lin Naing software and considered $P1 = 0.8$, $P2 = 0.65$, $\alpha = 0.05$ and $\beta = 90\%$ was determined as 827 and due to probability of participant's drop out, sample size was increased to 1000.

Women aged 20-50 years, married and volunteers or referred by health centres or physicians for screening of cervical cancer were chosen. The exclusion criteria were pregnancy or doubt about it, hysterectomy, previous cervical cancer or pre-cancerous lesions, cryotherapy, cautery or cone biopsy for treatment of cervical disease, previous radiotherapy, abnormal vaginal bleeding, the history of genital warts or herpes, using medication for genital disease and early menopause.

After approval from the Research Ethics Committee of Tabriz University of Medical Science, the investigator went to Alzahra therapeutic- educational centre and invited women that referred for Pap smear and had inclusion criteria for study. For this purpose, researcher completed the check list of participant's selection, then, the made questionnaire and approval form was given to participants in a private place and was asked to answer the questions. The content validity was used to acquire the scientific validity of socio- demographic and midwifery information questionnaire. For this purpose, the questionnaire was

given to 7 professors of Tabriz University of Medical Science to evaluate the content of questionnaire. After collecting their idea, needed changes was done and finally used for study.

In this study, first, the form of socio-demographic and midwifery information was completed, then Pap smear and DVI was done for all women. For this purpose, participants went on a gynecological bed and in lithotomic position. First, Pap smear was done with a plastic spatula for exocervix and a cytobrush for endocervix and sample expanded on a lamella and fixed with fixation solution (alcohol 95%). Then, the cervix exposed with 5% acetic acid by cotton swab for 30 seconds and observed under adequate light with magnifying glass.

Presence of acetowhite region in the cervix with sharp borders, abnormal finding in cervix such as polyp, leukoplakia or invasive cancer were considered as positive DVI. All women who had abnormality in DVI referred to colposcopy and biopsy.

The Pap smear results were reported after 2 week by hospital's pathologist and if was positive (Invasive cancer, ASC-US, ASC-H, LSIL, HSIL), the participants called for referring to colposcopy and biopsy. The result of biopsy was evaluated by pathologist and the results compared with each other.

Data analysis

Data were analyzed through descriptive and inferential statistical tests such as frequency and chi- square tests by using SPSS version 13 software. Their sensitivity, specificity, positive predictive value, negative predictive value, LR+, LR- and Confidence Interval were determined. P value less than 0.05 considered significant.

RESULTS

In this study, participant's mean (SD) of age and BMI were 33(7) and 27.20(4.95) respectively. 919(91.9%) of women were educated and 81(8.1%) were illiterate. Mean (SD) age of women in first intercourse was 20(4). Three participants were smoker and 4 women were alcohol user. Mean (SD) of menarche and first intercourse age were 19(4) and 26(7) respectively. 94.4% of women referred for routine Pap smear and 5.6% of women referred for genital disorders. These problems included mense problems, abdominal pain, vaginitis, infertility, post coital bleeding and etc [Table 1].

974(94.7%) cases were normal and had no findings and 26(2.6%) participants had positive results in Pap smear or DVI test. 12 women had abnormal Pap smear, 14 women had positive DVI and 1 woman had abnormality in both DVI and Pap test which referred to colposcopy and biopsy. Among women with abnormal Pap smear, 9 women had

Atypical Squamous Cells of Undetermined Significance (ASCUS) in Pap test and 3 women had Dysplasia, Atypical endocervical and Low grade Squamous Intraepithelial Lesion (LSIL) results. Among 14 women with positive DVI, 4 cases had HPV and Koilocyte in biopsy result. 1 women with abnormality in both method had carcinoma in biopsy that referred to oncologist. In this study the sensitivity and specificity of DVI was 71.4% and 50% while it was 14.3% and 50% for Pap test [Table 2].

DISCUSSION

Cervical cancer is one of the important health issues in many low resource settings and it is the third common female's cancer in the world.³ Almost 450000 new cases of cervical neoplasia are recorded annually. The prevalence of cervical cancer is high in countries that have poor screening programs.¹³ The screening failure is a major cause of cervical cancer mortality in developing countries, while it is preventable with screening programs.^{10,14} Different methods are available for cervical cancer screening.¹⁴ one of these methods is DVI with 5% of acetic acid. Due to the ability of DVI in cervical cancer identification, some studies suggest this method for screening.⁹ Pap smear is another method.¹⁵ Previous studies indicated that sensitivity of DVI in identification of pre-cancerous cervix lesions is more than Pap smear.¹⁶⁻¹⁸ For example, a study in Tehran showed that, sensitivity of DVI was 96% and its specificity was 44% that were higher than sensitivity and specificity of Pap smear that were 42% and 10% respectively.⁹ Another study in 2012, reported the sensitivity and specificity of DVI, 88.8% and 99.9% while they were 37.5% and 99.6% for Pap smear.¹⁹ In Saharsabuddhe, *et al.* study, the sensitivity and specificity of DVI was reported 80% and 82.6% that were higher than Pap smear (60.5% and 64.6% respectively).²⁰ Sensitivity of DVI in different studies was reported between 75 to 100%^{13-15,17} and its

specificity was reported between 16 to 85%.^{16-18,21} Also, it is reported that sensitivity of DVI is higher than Pap smear while its specificity is lower than Pap test.^{16,18,22,23} In our study sensitivity and specificity of DVI were 71.4% and 50% compared with 14.3% and 50% respectively for Pap smear. In different studies positive predicative value of DVI was reported higher than Pap smear.^{18,22} In our study positive and negative predicative value of DVI was reported 35.7% and 81.8% compared with 10% and 60% for Pap smear.

CONCLUSION

In this study DVI had higher sensitivity than Pap smear as like as other studies, but, in our study specificity of two methods was equal while it was reported different in previous studies. Pap smear is a method with lower sensitivity and its main failure reason is related to false sampling and interpretation.¹⁹ On the other hand, Pap smear requires laboratory facilities, cost and time that are especially more impressive in developing countries.^{9,19,24}

While DVI doesn't need any laboratory facilities and its result is obtained at the same visit²⁵ So patient's follow-up is more accessible.⁹ Since a diagnostic value of DVI is comparable to Pap smear, and it performs well in detecting a high grade lesion, we conclude that DVI could be used as a screening modality for cervical cancer in low resource settings.

One of the problems of DVI method is being a lot of criteria for interpretation of positive test results. Proper training of health care providers and physicians is the important criteria. In DVI method, if any acetowhite lesion is considered positive, there would be a lot of false positive results that could need to refer to oncologist and it is not feasible financially for poor people. So, proper training of health care providers is one of the strategies presented in this field.²⁶ Also in this method only exocervix is measurable,²⁷ so, it never can be used as an alternative method for Pap smear, only it can consider as a supplemental method.

This study was limited to females of Tabriz, Iran, thus it is recommended that other studies to be performed in different places of Iran. Lack of access to women's health records and trust to their statements was the second limitation of this study.

Table 1: The reasons of women's refer to Pap smear

Cause	Number (%)
Routine Pap smear	944 (94.4)
Menstrual problems	12 (1.2)
Abdominal pain	9 (0.9)
vaginitis	24 (2.4)
infertility	2 (0.2)
Post coital bleeding	7 (0.7)
Other reasons	2 (0.2)

Table 2: Sensitivity, specificity, PPV, NPV, LR+, LR- and CI of studies methods

Method	Sensitivity (%)	Specificity (%)	PPV (%)*	NPV (%)*	LR+ (%)*	LR- (%)*	CI (%)*
DVI	71.4	50	35.7	81.8	1.4	0.57	95
Pap smear	14.3	50	10	60	0.29	1.71	95

*PPV – Positive predictive value; *NPV – Negative predictive value; *LR+ – Positive likelihood ratio; *LR- – Negative likelihood ratio; *CI – Confidence interval

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