Original Article

Diagnostic Accuracy of Direct Visual Inspection with 5% Acetic Acid in Cervical Cancer Screening in Low Resource Settings

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Abstract

Objective: To determine the diagnostic accuracy of Direct visual inspection (DVI) with 5% acetic acid in cervical cancer screening.
Methodology: This Cross-sectional validation study was conducted in the Outpatient clinic of Obstetrics and Gynecology department of Kahuta Research Laboratories (KRL) hospital, Islamabad between 1st December 2017 to 31st May 2018. After fulfilling the inclusion/exclusion criteria, DVI was performed on women in the outpatient clinic and presence of acetowhite changes in the cervix was considered as positive DVI. Women with positive result with DVI, and those with negative DVI but abnormal looking cervix were called for colposcopic directed biopsy which was considered to be gold standard.2*2 table was constructed to analyse the results for sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy. Positive and negative likelihood ratios (PLR and NLR) were also calculated.
Results: Mean age of the study participants were 34.21 ± 6.32 years. 22 DVI +ve women, and 16 DVI –ve women but with abnormal looking cervix were sent for colposcopic directed biopsy. Biopsy confirmed 17 of the 38 cases of cervical intraepithelial neoplasia (CIN) I/II of which 14 were DVI +ve and 3 were DVI –ve. The sensitivity, specificity, PPV, NPV, PLR, NLR and diagnostic accuracy of DVI were 82.35%, 97.77%, 63.64%, 99.15%, 36.96, 0.18 and 97.07% respectively.
Conclusion: In a developing country like Pakistan where Pap smear is not available in low resource settings, DVI is a very helpful tool in picking up preneoplastic lesions due to its good diagnostic accuracy.
Key words: Cervical cancer, screening, visual inspection, acetic acid

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Introduction

Cervical cancer, being one of the most common malignancies of the genital tract, is affecting 490,000 women every year with a largest burden over the developing world, about 80%[1]. In a Pakistani population, it comprises 3.6% of all cancers.[1]The causative agent of the cervical cancer is human papillomavirus (HPV) infection in more than 90% of the cases. Most of the cases are in underdeveloped countries due to lack of awareness, ineffective screening strategies and fear of people because of positive results.[2,3] Different screening strategies have been devised to diagnose cervical cancer in its precancerous stages, of which Papanicolaou (Pap) smear is the standard one.[4] This screening helps in detecting cervical cancer in its precancerous stages so that early intervention can prevent its progression to malignant stages.[5]

Cervical cancer is affecting 1.36/10,000 population in Pakistan and presently only 1.9% of the population is being screened for it.[6] Due to non-availability of instruments and trained personnel for conducting Pap smear, multiple low cost screening strategies have been introduced in low resource settings like Direct Visual Inspection of the cervix after applying Acetic acid (DVI).[1,6]DVI is a very simple and cost effective method to differentiate between diseased and healthy cervix. So it can be used as a primary screening method in developing countries or where cytological testing services are suboptimal, because of its advantages of requiring a lower level of infrastructure and immediate

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results. World Health Organization (WHO) has also emphasized to consider DVI as an alternate to cytology for identifying people who are at risk of cervical cancer.[1,7,8]

In one study, DVI has sensitivity & specificity of 93.5%[1] & 95.8%[1] while in another study the sensitivity & specificity of DVI is 71.4% & 50%with prevalence of histologically proven cervical cancer varied from 43.2% in one population to 67% in other.[9,10] So this study was conducted to determine the diagnostic accuracy of DVI with 5% acetic acid in cervical cancer screening as previous literature is showing variability in its accuracy within 5-year studies.

Methodology

This cross sectional validation study was conducted in the Outpatient clinic of Obstetrics and Gynecology department of Kahuta Research Laboratories (KRL) hospital, Islamabad from 1st December 2017 to 31st May 2018. Ethical approval was taken from internal review board (IRB). Inclusion Criteria were married women between the age of 25-50 years. Exclusion Criteria included pregnancy, hysterectomy, previous history of cervical disease or any treatment of it. Women of reproductive age who present with gynaecological problems fulfilling the inclusion criteria were enrolled in the study. Verbal informed consent was taken. History and physical examination was performed and entered on proforma. Examination was performed in the outpatient clinic by the researcher. After visualizing the squamocolumner junction, 5% acetic acid was applied on cervix by cotton swab for 30 seconds. Appearance of acetowhite changes in the cervix was considered as positive DVI. Women with positive result with

DVI, and those with negative DVI but abnormal looking cervix were scheduled for colposcopy and biopsy. Sample size was calculated by taking sensitivity 93%, specificity 90%, prevalence 43%, precision for sensitivity 6%, precision for specificity 4%, confidence level 95%[9] and total sample size was 376.

All statistical data were analysed using Statistical Package for Social Sciences (SPSS) version 21 software. Mean +- SD was calculated for age. Frequency and percentages were calculated for TP (True positive), TN (True negative), FP (False positive), and FN (False negative).2X2 table was constructed to analyse the results for sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy. Positive and negative likelihood ratios (PLR and NLR) were also calculated.

Results

During the study period, 382 women were recruited for the study who fulfilled the inclusion criteria. 376 were eligible for randomization and underwent DVI. 6 patients were not taken into the study because of unsatisfactory screening results. Mean age of the study participants were 34.21 ± 6.32 years. 22 DVI +ve women, and 16 DVI –ve women but with abnormal looking cervix were sent for colposcopic directed biopsy. Remaining 338 women had negative DVI along with normal looking cervix and they were considered as true negatives and didn't require biopsy. Biopsy confirmed 17 of the 38 cases of CIN I/II of which 14 were DVI +ve and 3 were DVI –ve.

The sensitivity, specificity, PPV, NPV and diagnostic accuracy of DVI and abnormal looking cervix were 82.35% (95% [CI]: 56.57- 96.20), 61.90 % (95% CI: 38.44 - 81.89), 63.64% (95% CI: 49.29 - 75.91), 81.25 % (95% CI: 59.53 - 92.73), and 71.05% (95% CI: 54.10 - 84.58) respectively. PLR and NLR were 2.16 (1.20 - 3.89) and 0.29 (0.10 - 0.84). Overall validity was calculated by keeping aside 338. DVI negative cases as shown in Table I.

Table I: Validity of DVI.

	Biopsy (+)(-)		Total
DVI +ve	(a) 14 (TP)	(b) 8(FP)	22
DVI –ve with abnormal looking cervix	(c) 3 (FN)	(d) 13 (TN)	16
Total	17	21	38

Statistics	Formula	Value	95% CI
Sensitivity	a/(a+c) × 100	82.35%	56.57% - 96.20%
Specificity	d/(d+b) × 100	61.90 %	38.44% - 81.89%
PPV	a/(a+b) × 100	63.64%	49.29% - 75.91%
NPV	d/(d+c) × 100	81.25 %	59.53% - 92.73%
Positive likelihood ratio (PLR)	Sensitivity/1-specificity	2.16	1.20 - 3.89
Negative likelihood ratio (NLR)	1-sensitivity/ specificity	0.29	0.10 - 0.84
Diagnostic accuracy	a+d/a+b+c+d	71.05%	54.10% - 84.58%

After adding the negative findings too, the sensitivity, specificity, PPV, NPV, PLR, NLR and diagnostic accuracy of DVI were 82.35%, 97.77%, 63.64%, 99.15%, 36.96, 0.18 and 97.07% respectively. (Table II)

Table II: Validity of DVI after inclusion of negative findings.

	Positive biopsy	Negative biopsy(A)	Normal looking cervix and negative DVI (B)	Confirmed Negative finding(A+B)	Total
DVI +ve	(a) 14 (TP)	8	----	(b) 8 (FP)	22
DVI –ve with abnormal cervix	(c) 3 (FN)	13	338	(d) 351 (TN)	354
Total	3			373	376

Statistics	Formula	Value	95% CI
Sensitivity	a/(a+c) × 100	82.35%	56.57% - 96.20%
Specificity	d/(d+b) × 100	97.77 %	95.66% - 99.03%
PPV	a/(a+b) × 100	63.64%	46.01% - 78.23%
NPV	d/(d+c) × 100	99.15 %	97.67% - 99.69%
Positive likelihood ratio	Sensitivity/1-specificity	36.96	17.99 - 75.90
Negative likelihood ratio	1-sensitivity/specificity	0.18	0.06 - 0.50
Diagnostic accuracy	a+d/a+b+c+d	97.07%	94.83% - 98.53%

Discussion

Published literature has shown that if the women are screened for only once at 35 years of age, it can minimize the chances of cervical cancer by one quarter.[11]

Our study included women in the age reproductive age group. Khan et al and Denny also included the same age group in their study.[12,13] This is because majority of the women who have preinvasive cervical cancer lesions belong to this age group.

In present study, DVI was done by the gynaecology resident. In other studies, by Khan et al, Goel et al and Bharani B et al, gynecologists carried out the procedure.[12,14,15] In contrast, other trained healthcare professionals have also played their active role in few studies.[13,16] This is because of the feasibility of the procedure and its simple nature, as it can be conducted by any healthcare professional. That's how it can help people in underdeveloped countries to do screening even without trained people and advanced instruments.

In present study, DVI was done and in case of positive DVI or negative DVI with abnormal looking cervix, cervical biopsy was taken. Goel et al. did it in a similar way; but they performed LLETZ (large loop excision of transformation zone) in place of a biopsy. In a study by Khan et al, visual inspection with Lugols iodine (VILI) was done in addition to DVI and pap smear.[12]

When the different screening strategies have been combined, the diagnostic accuracy increases. However, in our study, confirmation of the positive results by DVI was done by colposcopy.

The DVI-positive results in our study were 5.85%. Goel et al. highlighted a bit higher rate for VIA, of about 12.5%. Cecchini et al. found VIA positive patients in one quarter of their sample size.[17] This much variability in the DVI positive patients may be because of the difference in analysis of the VIA results as some studies were conducted by paramedical staff while other studies were done by doctors.

Sritipsukho P et al compiled 11 studies, and found the overall sensitivity, specificity, PPV and NPV of VIA to be 71.8%, 79.4%, 16.7% and 99.0%.[18] Our study highlighted a better sensitivity (82.35%) as compared to other studies as this study was conducted by the doctors only and uniform criterion were used.

Other studies found a sensitivity of VIA in the range of 63-89% while specificity was in the range of 43-74% which is in contrast to the results of our study as our study found a higher specificity.[19] The PPV and NPV value of the DVI in current study was found to be 63.64% and 99.15% respectively. The high NPV rules out the CIN when it is not present. Shankaranarayanan R conducted a study in India, where the deaths by cervical cancer were reduced by 35% between the age group of 30-59 years. Other similar studies found reduced deaths due to cervical cancer when screened by VIA as compared to pap smear screening. So DVI was the preferred screening strategy in those studies.[20,21,22]

Pothisuwan M et al had also put emphasis over the importance of VIA that it may decrease the burden of unnecessary colposcopies which was in line with the results of our study.[23]

Nanda K et al highlighted the sensitivity and specificity of Pap smear to be 47% (range 30-87%) and 95% (range 86-100%) respectively.[24] These results showed comparable sensitivity and specificity to DVI, but DVI picks up more severe dysplasia. The overall diagnostic accuracy of DVI came out to be 97.07% in present study.

Recent studies have again questioned the diagnostic accuracy of DVI and randomized controlled trials have been conducted to reconfirm its diagnostic accuracy.[25,26]

The one drawback of Pap smear that has been seen in clinical settings is that, some patients never come back to take their reports or for follow up so it delays the treatment given to those patients. The benefit of DVI is that it picks up precancerous lesions without involving any laboratory reports and that is more feasible for the patients to get the screening report on one visit without any delay in diagnosis.

Conclusion

In underdeveloped countries like Pakistan, DVI can be a useful technique in ruling out pre-neoplastic lesions due to its good diagnostic accuracy

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