VISUAL SCREENING WITH ACETIC ACID AND LUGOL'S IODINE- A BETTER OPTION FOR EARLY DETECTION OF CERVICAL INTRAEPITHELIAL NEOPLASIA

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ABSTRACT

BACKGROUND

Visual inspection based screening tests such as visual inspection with dilute acetic acid 4% (VIA) and with Lugol's iodine- VILI have been proposed as alternatives to cytology in mass screening program. To date there is only limited information on the accuracy of these tests in detecting high-grade squamous intraepithelial lesions (HSIL).

MATERIALS AND METHODS

This is a descriptive study done in Mahatma Gandhi Medical College and Hospital from July 2014 to June 2016. Total no. of women screened were 4405. Out of them 14% were positive on VIA, 16.2% were positive on VILI and 12 were diagnosed with HSIL. Sensitivity, specificity, positive and negative predictive values for VIA were 94.1%, 86.0%, 2.5% and 99.9% and sensitivity, specificity, positive and negative predictive values for VILI were sensitivity 82.3%, specificity 84%, PPV 2.0% and NPV 99.9%. Both VIA and VILI had a significant higher sensitivity and specificity. Both tests were accurate visual tests for use in screening and treatment programme in low resource settings.

RESULTS

This study was carried out during July 2014 to June 2016. A total of 4405 women were screened. Out of 4405 women, 14% were VIA positive and 16.2% were VILI positive. Out of VIA positive, Biopsy was taken. Out of VIA positive 83% were normal, 39 had low-grade lesion i.e. 6.9% and 16 had HSIL i.e. 2.5%. In VILI positive women, 36 had low-grade lesion and 11 had HSIL and 3 were having invasive carcinoma.

CONCLUSION

Sensitivity, specificity, positive and negative predictive values for VIA were 94.1%, 86.0%, 2.5% and 99.9% and sensitivity, specificity, positive and negative predictive values for VILI were sensitivity 82.3%, specificity 84%, PPV 2.0% and NPV 99.9%. Both VIA and VILI had a significant higher sensitivity and specificity. Both tests are accurate visual tests for use in screening and treatment programme in low resource settings.

KEYWORDS

Visual Inspection Acetic Acid, Lugol's Iodine, VIA, VILI, Accuracy, Sensitivity, Specificity, Cervical Neoplasia and Screening.

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BACKGROUND

Cancer of cervix uteri is the most common cancer among women in the developing world. In developing countries like India and Africa, in low resource settings¹ simple and inexpensive tests are available for detection of precursor lesion such as VIA (Visual inspection of cervix with 4% to 5% acetic acid) and VILI (Lugol's iodine application).

Screening programs exist in few countries, where reduction in mortality from cervical cancer has been observed.^{2,3} In India, in collaboration with the national institutions to estimate and compare the sensitivity and specificity of VIA and VILI to detect (HSIL) and to study the

accuracy of these screening tests in relation to age group, education, marriage, number of pregnancies, menopausal status and visibility of SCJ (Squamocolumnar Junction).

Study Design

This is a descriptive study done during 2014 to 2016, a study of cervical cancer screening was conducted in India, Jaipur in Mahatma Gandhi Medical College and Hospital.

All women participating in the study were tested with screening test VIA and VILI, and reference investigation namely colposcopy. Biopsies were taken in women with abnormal or suspicious findings on colposcopy. Positive disease was defined as HSIL and reference gold standard was histopathology.

Participants

They were healthy symptomatic women, ambulatory, aged 25 - 45 years with an intact uterus and having no history of cervical cancer. A female health worker was appointed for the study and the subject attended open screening program. A printed form was duly signed by participants.

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Test Procedures

VIA and VILI were performed by trained health workers under supervision of doctor. Health workers and medical professionals were given a training of VIA and VILI and Colposcopy using lectures, discussions, review of photograph of normal and abnormal cervix.⁴

In outdoor, each woman was tested with VIA followed by colposcopy and VILI was performed on an examination table. Cervix was exposed by inserting a bivalve speculum. After applying 4% acetate acid to cervix, examination was done after one minute under vision of halogen lamp and then colposcopy was done. In VIA positive cases a punch biopsy was taken from abnormal area and sent for histopathological examination. Final diagnosis was based on histopathology, i.e. gold standard to find out true disease.

For cervical neoplasia, colposcopy and directed biopsy are commonly used and are accepted reference standard ("gold standard") investigations.^{5,6,7}

If histology is not available, then colposcopic diagnosis may be accepted as true disease.^{6,7}

Statistical Methods

HSIL were considered as true positive disease to calculate sensitivity, specificity and predictive values of the screening tests in order to obtain conservative estimates of accuracy to avoid spectrum bias.⁸

MATERIALS AND METHODS

During 2014 to 2016, a study of cervical cancer screening was conducted in India, Jaipur in Mahatma Gandhi Medical College and Hospital. 4405 women were recruited attending outdoor in Mahatma Gandhi Hospital. All women participating in the study were tested with screening test VIA and VILI and reference investigation namely colposcopy. Biopsies were taken in women with abnormal or suspicious findings on colposcopy. Positive disease was defined as HSIL and reference gold standard was histopathology.

RESULTS

Participants

VIA HISTO		1. Negative	2 Positive	3 Invasive Cancer	Total	%
0	Not done	0	2		2	0.3%
1	Inflammation/ Chronic Cervicitis	46	163		209	34.6%
2	Squamous metaplasia	36	163		199	33.0%
3	HPV infection	12	48		60	9.9%
4	Atypia	3	13		16	2.6%
5	CIN 1	3	39		42	6.9%
6	CIN 2	0	6		6	0.9%
7	CIN 3	0	6		6	0.9%
8	Early invasive carcinoma	0	2		2	0.3%
9	Invasive squamous cell carcinoma	1	2		3	0.4%
10	Invasive adenocarcinoma	0	0		0	0.0%
99	Others	16	42		58	9.6%
Total		117	486		603	100.0%

Table 3. Histopathology X Findings of VIA

- Sensitivity (94.1%)
- Specificity (86.0%)
- Positive Predictive Value (2.5%)
- Negative Predictive Value (99.9%)

My study was carried out during July 2014 to June 2016. A total of 4407 women who were attending gynae outdoor were recruited, out of 4407 women 2 women refused for VILI test.

Squamocolumnar Junction	No. of Women	%
Yes, fully seen	4360	98.9%
Yes, partially seen	39	0.9%
Not seen	8	0.2%
Total	4407	100%

Squamocolumnar Junction Frequency

Table 1

As the Table 1 suggests out of 4407 squamocolumnar junction was fully visualised in 4360 women i.e. 98.9%; in 8 women squamocolumnar junction was not visualised and in 39 women SCJ was partially visualised.

VILI Results	No. of Women	%
Negative	3693	83.8%
Positive	712	16.2%
Invasive Cancer	0	0%
Total	4405	100%

Finding of VILI Results

Table 2

VIA Results	No. of Women	%
Negative	3719	86%
Positive	603	14%
Unknown	0	0%
Total	4322	100%

Finding of VIA Results

VIA was positive in 603 women i.e. 14% and VILI was positive in 712 women i.e. 16.2%. Test positivity was related to visibility of SCJ, age, menstrual status, education, marital status and pregnancies. Out of VIA positive 486 cases 408 were normal, i.e. 83%. 39 had low-grade lesions i.e. 6.9% and 16 have HSIL i.e. 2.5%. Among women tested with VILI, out of 486 VILI positive women 408 were normal i.e. 83%. 36 had low-grade lesion and 11 had HSIL and 3 were having invasive carcinoma. Women were treated after result of histopathology, because it is a gold standard test.

Sensitivity of VIA in detecting HSIL was 94.1% and specificity was 86%, PPV was 2.5% and NPV was 99.9%.

VILI HISTO		1 Negative	2 Positive	3 Invasive Cancer	Total	%
0	Not done	0	2		2	0.4%
1	Inflammation/ Chronic cervicitis	42	167		209	34.6%
2	Squamous metaplasia	35	164		199	33.3%
3	HPV infection	12	48		60	9.9%
4	Atypia	2	14		16	2.6%
5	CIN 1	6	36		42	6.9%
6	CIN 2	0	6		6	0.9%
7	CIN 3	1	5		6	0.9%
8	Early invasive carcinoma	02	2		2	0.3%
9	Invasive squamous cell carcinoma	0	1		3	0.4%
10	Invasive adenocarcinoma	17	0		0	0.0%
99	Others	117	41		58	9.6%
Total		117	486		603	100.0%

Table 4. Histopathology X Findings of VILI

- Sensitivity (82.3%)
- Specificity (84.0%)
- Positive Predictive Value (2.0%)
- Negative Predictive Value (99.9%)

DISCUSSION

A screening test is good because of its safety, simplicity and its accuracy which is measured by sensitivity and specificity.⁹ A suitable reference test should distinguish the subjects who are truly positive from those who are negative. A study will suffer from “verification bias” if the reference investigation is restricted to test positive individuals only to a sample of test negative persons, such bias is known to inflate sensitivity estimates and may be avoided if all individuals receive the reference investigation irrespective of the test results.¹⁰ Previous cross-sectional studies¹¹ have reported to the accuracy of VIA, but all except 2 studies^{6,12} suffered from verification bias.

There are no published results of VILI in recent decades, but VILI had significantly higher sensitivity and specificity than those reported for VIA in Zimbabwe⁶ and Chinese¹² studies. The characteristics of VIA as a screening test have been established by many cross-sectional studies. VILI is used to detect colour pattern by health workers.

Though sensitivity and specificity of VIA and VILI have not much far difference, but if compared VIA is most specifically cheap and simple procedure. It can be done in outdoor by paramedical staffs also and can be used for larger population.

CONCLUSION

Sensitivity, specificity, positive and negative predictive values for VIA were 94.1%, 86.0%, 2.5% and 99.9% and sensitivity, specificity, positive and negative predictive values for VILI were sensitivity 82.3%, specificity 84%, PPV 2.0% and NPV 99.9%. Both VIA and VILI had a significant higher sensitivity

and specificity. Both tests are accurate visual tests for use in screening and treatment programme in low resource settings.

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