ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 04 | April - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

CONCURRENT EFFICACY EVALUATION OF CONVENTIONAL CYTOLOGY, VISUAL INSPECTION WITH ACETIC ACID(VIA) AND HPV-DNA TESTING IN SCREENING OF PREMALIGNANT LESIONS OF CERVIX IN TERTIARY HOSPITAL IN TRIPURA

Obstetrics & Gynaecology

Dr. Dibakar Debbarma MS Obs & Gynae, B.S.M Hospital Kamalpur, Dhalai, Tripura

Dr. Jahar Lal Baidya* M.D, Obs & Gynae, Professor, Dept. of Obstetrics & Gynaecology, Agartala Govt. Medical College, Agartala, Tripura, India. *Corresponding Author

Dr. Salil Bindu Chakraborty M.D Obs & Gynae, Associate Professor, Dept. of Obstetrics & Gynaecology, Agartala Govt. Medical College, Agartala, Tripura,India.

Dr. Abhijit Datta M.D, Pathology, Professor, Dept. of pathology, Agartala Govt. Medical College

ABSTRACT

Aim To find out the validity of Visual Inspection with Acetic Acid (VIA), HPV-DNA in screening of premalignant cervical lesions. **Objectives** 1>To evaluate feasibility of screening tools Visual Inspection with Acetic Acid (VIA) and HPV-DNA in detection of premalignant lesions of cervix. 2>To evaluate simultaneous testing feasibility of screening tools of Visual Inspection with Acetic Acid (VIA) and HPV-DNA in detection of premalignant lesions of cervix taking PAP smear of as gold standard. **Material and method-** Cross-Sectional Study was done in Department of Obstetrics and Gynaecology OPD, Agartala Govt. Medical College & GBPH from JANUARY 2018 to JUNE 2019, Women aged between (30-65 years) years attending Obstetrics and Gynaecology Out Patients Department; total 360 patients were subjected for study. **Result-** A total of 360 women aged 30–65 years participated in this study; 43.6% of the women were aged 30–40 years,33.6% of the women 41-50 years and 22.7% of the women were aged 51-65 years. In this study total Pap positive is 63(17.5%), Pap negative 82.5 %. PAP positive case includes LSIL 6.11 %, HSIL 6.94 %, malignancy 3.88 %.HPV-DNA positive cases are 87 (24.16%) and negative cases are 273 (75.83%). VIA positive (20%) and 288 women were negative VIA. VIA compared to final diagnosis was 57.14% with specificity of 89.89%, PPV of 48.27% and NPV of 77.16% .HPV-DNA compared to final diagnosis was 83.66% with specificity of 89.22%, PPV of 56.16% and NPV of 76.58% .The net sensitivity of both HPV DNA and VIA compared to final diagnosis 95%, specificity 80.1%, PPV 50.42%, NPV 98.75%. **Conclusion-** The role of pap smear for cervical cancer screening has long been established in the West but it is not a very feasible test for a resource limited setting. Alternative methods such as VIA may be very useful in a resource limited setting but VIA has low sensitivity and may not perform well as stand-alone tests, so adjunctive tests are one way of improving specificity of the test.

KEYWORDS

INTRODUCTION

Cervical cancer causes more than a quarter of a million deaths worldwide, with527,600 new cases diagnosed in 2012, but more than 90% occur in lower and middle-income countries or regions without the infrastructure and trained personnel to deal with the condition [1,2]. Global estimates are projected to rise by 25% in the next decade, if screening and treatment coverage are not increased. But more women die from this cancer in India, where most cases are detected at advanced disease states, than anywhere else in the world. In 2010, there were 141,768 new cases, with 77,100 deaths, accounting for nearly 20% of all cancer deaths in women from age 30-69. GLOBOCAN 2012 shows reduction in incidence and mortality at 122,844 cases and 67,477 deaths respectively [1,2]. Population based cancer registry program has registered 726 cases of cancer among women in Tripura during 2011. Among them 161 had carcinoma cervix followed by 107 breast cancers[3].

In the US and in India, two naming systems are important in cervical cancer determination via cytology or histology. Squamous dysplasia is first categorized through cytology with the Pap test as either mild or severe dysplasia. Mild dysplasia is categorized as ASC-US, atypical squamous cells of unknown significance, or LSIL, low- grade squamous intraepithelial lesion) while severe dysplasia is divided ASC-H, "cannot rule out HSIL;" HSIL, high-grade squamous intraepithelial lesion; or CIS, squamous carcinoma *in situ*. Histology or tissue sample analysis, uses the following three stage classification of cervical intraepithelial neoplasia (CIN): CIN1, CIN2, and CIN3. The latter two or CIN2+ are at the highest risk, if undetected or untreated, to advance to cancer. However, in non-immunocompromised women, 10-20 years can pass before premalignant lesions transform to cancer and before it becomes possibly invasive and fatal. CIN1 on the other hand may resolve on its own, as is the case in most infections in women, especially those younger than 25[4–7].

Cervical cancer detection follows the process of screening, diagnosis, and treatment. In the US, according to the guidelines set by the American College for Obstetricians and Gynecologists (ACOG), gold standard practice calls for the following order: Papanicolaou smear or Pap test (cytology), HPV-DNA test (genotyping), colposcopy, biopsy and treatment for patients who are deemed positive for precancerous or cancerous lesions. A patient goes through these steps with some room for adjustment with adjunct co-testing, which is now encouraged; specifically, gynecologists should use the HPV-DNA test along with the Pap test to interpret either inconclusive results or mild dysplasia observable in colposcopy. Along with the change in co-testing, though routine testing using a Pap test is recommended, the frequency was reduced with new guidelines released in 2013 for most age groups. An abnormal Pap test is usually followed up by colposcopy, a form of cervix visualization using a colposcopy, or a type of low-power light microscope, that includes a green illumination filter for changes in tissue reflectance that can be enhanced with the use of contrast agents like acetic acid or Lugol's iodine. The instrument remains directly outside of the patient's vaginal opening and a speculum is used to expand the vagina to allow observation of the cervix. In addition to assessment of abnormal screening results, the procedure is used to assess genital warts on the cervix, cervicitis, polyps or benign growths, or if there is pain or bleeding. Because of low specificity associated with visualization, biopsy or histologic confirmation of abnormal sites follows colposcopy[8,9].

However, the burden in middle and low-income countries has different barriers compelling a different protocol. The WHO has continued to provide several possible frameworks to increase screening coverage that optimizes cost, training, and number of visits. In a minimum resource environment, testing should involve visual inspection with acetic acid (VIA) and at maximum, the screening regiment should involve VIA, cytology (Pap test), and HPV test [4,7].

METHODOLOGY

AIM

To find out the validity of Visual Inspection with Acetic Acid (VIA), HPV-DNA in screening of premalignant cervical lesions.

OBJECTIVES

1>To evaluate feasibility of screening tools Visual Inspection with

Acetic Acid (VIA) and HPV-DNA in detection of premalignant lesions of cervix.

2>To evaluate simultaneous testing feasibility of screening tools of Visual Inspection with Acetic Acid (VIA) and HPV-DNA in detection of premalignant lesions of cervix taking PAP smear of as gold standard.

MATERIALS AND METHOD

Study Design-
Cross-Sectional Study.

Study Setting-
Department of Obstetrics and Gynaecology OPD, Agartala Govt. Medical College & GBPH.

Study Duration-
JANUARY 2018 to JUNE 2019

Study Population-
Women aged between (30-65 years)[14] years attending Obstetrics and Gynaecology Out Patients Department.

Sample Size: $n = \frac{4pq}{L^2} = \frac{4\times66\times34}{25}$

p = Prevalence of VIA = 66% [15]
q = (100 – p)
L = Absolute error = 5%

= 360

Inclusion Criteria:
women aged between (30-65) years attending Obstetrics & Gynaecology Out Patient Department with gynaecological complaints has subjected for study.

Exclusion Criteria:
1. History of previous cervical lesion, received treatment for precancerous and cancerous lesions of cervix.
2. Unmarried women.
3. Pregnant women.
4. Puerperal women.
5. Not willing for screening.

Data Collection Procedure: -
After getting approval of the institutional ethical review committee the study has started. Women attending outdoor department of obstetrics and Gynaecology fulfilling inclusion &exclusion criteria, is included in this study and informed consent is taken from each patient. Demographic information is collected.

History &general physical examination has performed. Gynecological speculum examination is performed with patients in dorsal recumbent position, cervix will be visualized with a Cusco's speculum(Naked eye inspection),followed by taking of Pap smear using spatula & Cyto-brush, HPV-DNA sample collection with cyto-brush and then 3 -5% acetic acid is applied on cervix using cotton swab& observation has noted after 1 minute. If a well- defined dense opaque acetowhite lesion close to the squamocolumnar junction or acetowhite area close to the transformation zone is observed, the result has labeled positive. All the data was collected and recorded in a Proforma attached at the end.

Reference Standard And True Disease-
The reference standard for defining final disease status was PAP smear. Disease status was assessed on the basis of PAP smear report. True disease was defined as PAP smear report confirmed LSIL/HSIL. Cases of invasive cancer were excluded from the analysis in order to obtain conservative estimates of test accuracy.

Data Analysis: -
Data was entered in SPSS version 20 and analysis was done for finding out sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV).

RESULT AND ANALYSIS

A total of 360 women aged 30–65 years participated in this study; 43.6% of the women were aged 30–40 years,33.6% of the women 41-50 years and 22.7% of the women were aged 51-65 years. The age distribution of the participating women is given in Table 1.

Most of the women had some level of education, having attended primary school (34.44%), secondary school (59.44%), or high school (3.88%), and 1% were graduates. The education level of participant women is given in table no 2.

In this study para 2 women having maximum no (76.38%) followed by para 3 (11.94%), para 1(7.5%), para 4(3%), para 5(0.55%), para 6(0.27%), nullipara (0.27%). The reproductive characteristics of the participating women has shown in table no. 3

Distribution of the participant women according to their occupation has shown in table no.4

Distribution of the participant women according to their marital status has shown in table no .5

In this study, most of the women came here with the complaints of vaginal discharge 38% followed by itching external genitalia 19%, abnormal uterine bleeding 16%, chronic pelvic pain 11%, post-menopausal bleeding 10%, post coital bleeding 3% and pain during intercourse 3 %.Distribution of the women according to their complaints has shown in table no.6.

In my study total Pap positive is 63(17.5%), Pap negative 82.5 %. PAP positive case includes LSIL 6.11 %, HSIL 6.94 %, malignancy 3.88 %. Pap negative includes atypical glandular cell 0.55 %, bacterial vaginosis 1.11 %, ASC-US 6.94 %, reactive cellular changes associated with inflammation 13.33%, superficial and intermediate squamous cell without atypia 55%, trichomonas vaginalis 1.11 %. Not satisfactory cases only 1.11 %. PAP smear test positive cases were follow-up as per the institutional protocol of management of screen positive cases. Conventional Cytology Result has shown in table no.7,8,9 & chart no.2

Total 360 women were screened for HPV-DNA test. Out of 360 women HPV-DNA positive cases are 87 (24.16%) and negative cases are 273 (75.83%).out of 87 positive cases in 52 cases typing has been done. Out of 52 subtyping cases HPV-16 found in 29 cases (55.7%), HPV-18 found in 10 cases (19.23%), HPV-35 found in 8 cases (15.38), HPV-33 found in 5 cases (9.61%). HPV-DNA result has shown in table no.10.

In this study total 360 women were screened with VIA. Out of 360 women 72 women were positive VIA (20%) and 288 women were negative VIA. Those who are VIA Positive they were again schedule for cervical biopsy from acetowhite area. Out of 72 VIA positive invasive carcinoma having 10 cases, HSIL 12 cases, LSIL is 16 cases, chronic cervicitis 33 cases,1 squamous metaplasia and 1 case of condyloma found.(shown in table no.11).

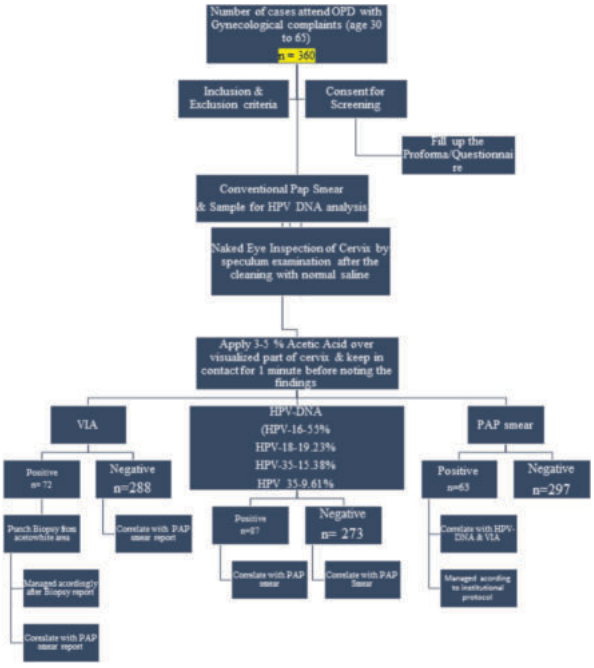
In the present study 14 cases of invasive carcinoma found and it has been excluded for prevention of data error. VIA test findings revealed 58 positives out of 346 (excluded 14 cases of invasive carcinoma) and 288 negatives cases.in 58 VIA positive cases reference standard test have diagnosed only 28 cases as premalignant and 30 cases were negative for premalignant lesions.

Out of 288 VIA negative cases,21 cases were diagnosed as premalignant lesions (LSIL & HSIL). Biopsy positive cases they were treated accordingly to the institutional protocol of treatment of invasive cancer. Based on these findings the sensitivity of VIA compared to final diagnosis was 57.14% with specificity of 89.89%, PPV of 48.27% and NPV of 77.16% given in Table no 13.

In this study, HPV-DNA test has been found positive in 73 cases and negative in 273 cases out of 346 participant women (out of 360 cases 14 cases excluded). In HPV-DNA positive cases out of 73 standard reference tests has been diagnosed premalignant 41 cases and test negative found in 32 cases. Out of 273 HPV-DNA negative test cases, 8 cases were diagnosed as premalignant lesions. Based on these findings the sensitivity of HPV-DNA compared to final diagnosis was 83.66% with specificity of 89.22%, PPV of 56.16% and NPV of 76.58% given in Table no 13.

The net sensitivity of both HPV DNA and VIA compared to final diagnosis 95%, specificity 80.1%, PPV 50.42%, NPV 98.75%.(Table no.15).

DISCUSSION



Invasive cervical cancer is preceded by a long premalignant phase known as cervical intraepithelial neoplasia. The goal of cervical cancer screening is the detection and treatment of precancer before cancer develops.[32] To detect cervical intraepithelial neoplasia LSIL and HSIL, which are considered to be true precancerous lesions, we need a well implemented secondary prevention system that provides screening for all women as well as treatment of detected abnormalities according to local policy. The Papanicolaou (Pap) smear has been shown to be highly effective in developed countries that have widespread screening programs.[11]

In low- & middle-income countries, because of the lack of trained cytotechnologists and cytology laboratories, there is often a long interval (1–1 1/2 months) between the Pap screening and when the test result is available. Additionally, only a small percentage of women with positive Pap smears have diagnostic evaluation and treatment, because of the lack of health centers that are able to treat preinvasive lesions. These problems with Pap smears have stimulated research on alternative tests, including visual inspection with acetic acid (VIA). VIA has demonstrated high sensitivity for detecting precancerous lesions and invasive cancer, but it is limited by low specificity. VIA is based on aceto whitening, with cervix turning white when exposed to 5% acetic acid. VIA has the advantage of requiring only low-technology equipment, and the result is available within a couple of minutes. These characteristics make VIA a realistic alternative for low-resource settings.[11]

Within the past five years, guidelines recognizing the value of HPV testing in both primary cervical screening and in the management of abnormal cervical cytology have been established in the US and are being considered in Europe. This trend has occurred because of the definitive association of high-risk HPV with cervical cancer and the overwhelming evidence that the sensitivity of high-risk HPV testing for lesions with a diagnosis of cervical intraepithelial neoplasia grade 2 or more severe (CIN 2+) is substantially higher than that of cytology.[10] Hence, the present study was planned to assess the test performance of HPV DNA testing and VIA for detection of high grade cervical intraepithelial lesions and also to assess the performance when HPV DNA testing and VIA are combined to find out the probable best screening option.

In this study, a total of 360 women aged 30–65 years participated in this study; 43.6% of the women were aged 30–40 years,33.6% of the women 41-50 years and 22.7% of the women were aged 51-65 years. These findings were almost similar with a study[50] done in Bangalore institution to assess the interobserver variability of VIA between nurse and physician wherein, maximum number of women (42.6%) were in this age group.

In this study, most of the women had some level of education, having attended primary school (34.44%), secondary school (59.44%), or high school (3.88%), and 1% were graduates. A study[13] from Andhra Pradesh reported 69.4% women with no formal education whereas a study[12] from Mumbai reported 78% literate women. The educational status of the women enrolled in this study was better when compared to the other studies that is, only 0.277 % women were illiterate in this study.

In this study, most of the women came here with the complaints of vaginal discharge 38% followed by itching external genitalia 19%, abnormal uterine bleeding 16%, chronic pelvic pain 11%, post-menopausal bleeding 10%, post coital bleeding 3% and pain during intercourse 3 %. The common presenting complaint was persistent white discharge per vagina seen in 64.2%. A study[17] from AIIMS, New Delhi reported vaginal discharge in 80 women, irregular vaginal bleeding in 13 women and post coital bleeding in one woman. In another study[16] from Bangalore institution persistent white discharge per vagina was the commonest complaint (64.2%) followed by post-menopausal bleeding in 6.6% and postcoital bleeding in 5.6%, its almost similar to our study.

In a study **Singh A et al**. Pap smear was positive in (12.2%) and negative in 87.8%. PAP positive cases included 9 cases of ASCUS/ASCUS-H, 12 cases of LSIL and 5 of HSIL. In this study total Pap positive is 63(17.5%), Pap negative 82.5 %. PAP positive case includes LSIL 6.11 %, HSIL 6.94 %, invasive carcinoma 3.88 %. Pap negative includes atypical glandular cell 0.55 %, bacterial vaginosis 1.11 %, ASC-US 6.94 %, reactive cellular changes associated with inflammation 13.33%, superficial and intermediate squamous cell without atypia 55%, trichomonas vaginalis 1.11 %. Not satisfactory cases only 1.11 %.[18]

Total 360 women were screened for HPV-DNA test. Out of 360 women HPV-DNA positive cases are 87 (24.16%) and negative cases are 273 (75.83%). Based on these findings the sensitivity of HPV-DNA compared to final diagnosis was 83.66% with specificity of 89.22%, PPV of 56.16% and NPV of 76.58%.

Sudula M, et al A population-based sample of 5603 women from Medchal Mandal in Andhra Pradesh, India were invited to participate in a study comparing Pap cytology, VIA, and HPV DNA screening for the detection of CIN3+. HPV testing had a higher sensitivity (100%) and specificity (90.6%).[19]

Surendra S. Shastri et al. Concurrent evaluation of visual, cytological and HPV testing as screening methods for the early detection of cervical neoplasia in Mumbai, India. Bull World Health Organ has shown that HPV DNA sensitivity and specificity for detection of precancerous lesion is 62.0%,93.5%. compared to our study HPV DNA sensitivity is much more in our study and specificity is almost same as their study.[20]

Surendra S. Shastri et al. Concurrent evaluation of visual, cytological and HPV testing as screening methods for the early detection of cervical neoplasia in Mumbai, India has argued that sensitivity of VIA 59.7% and specificity of VIA is 88%.compared to our study the sensitivity and specificity of VIA is almost same with this study for detection of precancerous lesions of cervix.[20]

Albert SO, et al a comparative study of visual inspection of the cervix using acetic acid (VIA) and Papanicolaou (Pap) smears for cervical cancer screening has shown that the sensitivity and specificity of VIA to detect for precancerous cervical lesions is 60%, 94.4%, positive predictive value 50%, negative predictive value 99.4%, and accuracy was 98.6%. compare to this study its almost same with our study.[21]

Smita Asthana et al., Evaluation of Co-Testing of Cervical Screening Tests in Detection of High Grade Cervical Intraepithelial Neoplasia has argued that Co testing of HPV-DNA and VIA can detect cervical precancerous lesion with the sensitivity of (VIA + HPV) 53% and specificity 91.6%.compared this study with our study co testing result net sensitivity 93.88% and net specificity 80.13 %.[22]

Surendra S. Shastri et al. Concurrent evaluation of visual, cytological and HPV testing as screening methods for the early detection of cervical neoplasia in Mumbai, India has argued that co testing with HPV and VIA for detection of precancerous lesions sensitivity is 90.0%, specificity 99.1%, PPV 34.7%, NPV 99.1%.

compared to our study is show that net sensitivity is 93.88% and specificity 80.13%, PPV 43.81%, NPV 98.76%.[20]

Chinoy R, et al. India has argued that the sensitivities of cytology, HPV testing, VIA, VIAM and VILI were 57.4%, 62.0%, 59.7%, and 75.4%, respectively (differences were not statistically significant). The specificities were 98.6%, 93.5%, 88.4%, and 84.3%, respectively. Adding a visual test to cytology or HPV testing in parallel combination resulted in a substantial increase in sensitivity, with a moderate decrease in specificity. The parallel combination of VILI and HPV testing resulted in a sensitivity of 92.0% and a specificity of 79.9%.[23]

The use of both VIA and VILI may be considered where good quality cytology or HPV testing are not feasible. The sensitivity of cytology and HPV testing increased significantly when combined with VIA or VILI.

In conclusion, as a single test, HPV was associated with the best balance of sensitivity, specificity and predictive values, on the basis of our findings. But HPV DNA testing is costlier, it is not possible in a low resource setting like in developing country for mass screening. Visual tests constitute a promising approach in low-resource settings and evidence from on-going studies on their ability to reduce incidence of and mortality from cervical cancer is crucial [2,42].

Testing with acetic acid may be considered for early detection of cervical neoplasia in settings where provision of good quality cytology or HPV testing is not feasible in view of technical, personnel, infrastructure and financial constraints. The sensitivity of HPV testing increased significantly by adding a visual test, such as VIA and the cost implications of these approaches remain to be established. However, this study was conducted in a single centre of Tripura, a small state of North East India with mixed population over a short period of time (one and half year). Further studies on a large scale with multi centric analysis is needed to validate the result in a better way.

CONCLUSION

In the present study of the 360 women VIA, and HPV DNA test was positive results in 20 % and 24.16%. PAP smear positive in 17.5 %. The PAP smear positive cases include LSIL 6.11 %, HSIL 6.94 %, invasive carcinoma 3.88 %. Pap negative includes atypical glandular cell 0.55 %, bacterial vaginosis 1.11 %, ASC-US 6.94 %, reactive cellular changes associated with inflammation 13.33%, superficial and intermediate squamous cell without atypia 55%, trichomonas vaginalis 1.11 %. Not satisfactory cases only 1.11 %.

The sensitivity of VIA compared to final diagnosis was 57.14% with specificity of 89.89%, PPV of 48.27% and NPV of 77.16%. The sensitivity of HPV DNA test compared to final diagnosis was 83.66% with specificity of 89.22%, PPV of 56.16% and NPV of 76.58%. The net sensitivity of both HPV DNA and VIA compared to final diagnosis 95%, specificity 80.1%, PPV 50.42%, NPV 98.75%.

Cervical cancer accounts for the highest number of deaths due to cancer among women in India. The role of pap smear for cervical cancer screening has long been established in the West but it is not a very feasible test for a resource limited setting. Alternative methods such as VIA may be very useful in a resource limited setting but VIA has low sensitivity and may not perform well as stand-alone tests, so adjunctive tests are one way of improving specificity of the test, in this study the joint test qualities of VIA and HPV were compared and from our results we could conclude VIA followed by HPV test would be an effective efficacy approval to identify women who need further treatment.

Acknowledgements
We are thankful to faculties and post graduate students for their help

Declarations
Funding: nil

Conflict Of Interest: none

Ethical Approval: The protocol of this research work was approved by the Institutional Ethics Committee, Agartala Government Medical College.

Table 1. Age distribution of the participant women.

Age group	Frequency	Percentage (%)
30 – 40	157	43.6
41 - 50	121	33.6
51 – 65	82	22.8

Table 2. Education level of participant women.

Education status	Frequency	Percentage (%)
Illiterate	7	0.277
Primary	124	34.44
Secondary	214	59.44
Higher secondary	14	3.88
Graduation	1	0.277

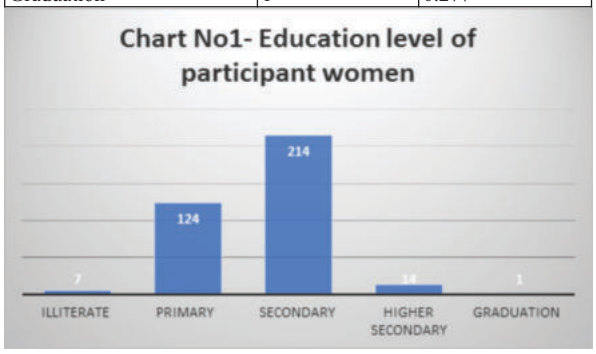


Table 3. The reproductive characteristics of the participating women.

Parity	Number	percentage
P0	1	0.27%
P1	27	7.5%
P2	275	76.38%
P3	43	11.94%
P4	11	3%
P5	2	0.55%
P6	1	0.27%
Grand Total	360	

Table 4. Distribution of the participant women according to their occupation.

Occupation	Frequency	Percentage (%)
Govt Employee	4	1.11
Health worker	2	0.55
House wife	351	97.5
Nurse	1	0.277
Sweeper	1	0.277
Teacher	1	0.277

Table 5. Distribution of the participant women according to their marital status.

Marital status	Frequency	Percentage (%)
Married	341	94.72
Widow	19	5.2

Table 6. Distribution of the women according to their complaints.

Complain	Frequency	Percentage (%)
AUB	57	15.83
Chronic pelvic pain	41	11.38
Dyspareunia	12	3.33
Itching external	69	19.1
genitalia	34	9.44
PMB	12	3.33
Post Coital Bleeding	135	37.5
Vaginal Discharge		

Table 7. Conventional Cytology Result

PAP smear result	Frequency	Percentage (%)
Negative	297	82.5
Positive	63	17.5

Table 8. Conventional Cytology findings (neoplastic)

PAP	Frequency	Percentage
ASC-US/ASC-H	25	6.94%
LSIL	22	6.11%
HSIL	25	6.94%
SCC	14	3.88%
ATYPICAL GLANDULAR CELL	2	0.55%

Table 9. Conventional Cytology findings (Others)

PAP	Frequency	Percentage (%)
Bacterial vaginosis	4	1.11
Not satisfactory	4	1.11
Reactive cellular changes associated with inflammation	48	13.33
Squamous metaplasia	14	3.88
Superficial and intermediate squamous cell without atypia	198	55
Trichomonas vaginalis	4	1.11
Table 9. Conventional Cytology findings (Others)		

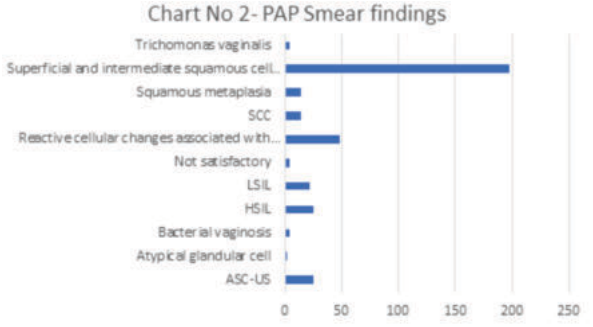


Table.10- HPV-DNA Result

HPV DNA testing results	Frequency	Percentage
HPV positive	87	24.16
HPV negative	273	75.83

Table 11. Visual Inspection with Acetic Acid

Visual inspection with acetic acid results	Frequency	Percentage
Positive	72	20
Negative	288	80

Table No 12.VIA results with final disease status as established by reference standard.

		Cervical PAP smear results	
		Positive	Negative
Visual inspection with acetic acid (VIA) results	Positive	28	30
	Negative	21	267

Table No 13-HPV-DNA results with final disease status as established by reference standard.

		Cervical PAP smear results	
		Positive	Negative
HPV DNA testing result	Positive	41	32
	Negative	08	265

Table No-14. Validity of screening tests for the detection of premalignant lesions of cervix (LSIL & HSIL) established by reference standard.

	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95%CI)
VIA	57.14% (53.18% to 62.1%)	89.89% (85.73% to 93.07%)	48.27% (45.51%to 50.95%)	77.16% (72.71% to 81.52%)
HPV DNA	83.66% (81.62% to 85.58%)	89.22% (87.54% to 90.86%)	56.16% (53.43% to 58.76%)	76.58% (73.8% to 78.39%)

Table No.15 Accuracy of combined screening tests for the detection of premalignant lesions of cervix (LSIL & HSIL) established by reference standard.

Simultaneous testing	Net Sensitivity (95% CI)	Net Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
VIA + HPV DNA testing result	93.88% (83.13% to 98.72%)	80.13% (75.14% to 84.52%)	43.81% (38.03% to 49.76%)	98.76% (96.36% to 99.56%)

REFERENCES-

1. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA Cancer J Clin. 2015 ;65(2):87–108.
2. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015 ;136(5):E359–86.
3. NCRP Anual Reports… [Internet]. [cited 2019 Sep 22]. Available from: http://ncdirindia.org/NCRP/Annual_Reports.aspx
4. World Health Organization, World Health Organization, Reproductive Health and Research. Comprehensive cervical cancer control: a guide to essential practice. [Internet]. 2014 [cited 2019 Sep 22]. Available from: http://apps.who.int/iris/bitstream/10665/144785/1/9789241548953_eng.pdf?ua=1
5. Solomon D, Davey D, Kurman R, Moriarty A, O'Connor D, Prey M, et al. The 2001 Bethesda System: terminology for reporting results of cervical cytology. JAMA. 2002 ;287(16):2114–9.
6. Krishnan S, Madsen E, Porterfield D, Varghese B. Advancing Cervical Cancer Prevention in India: Implementation Science Priorities. The Oncologist. 2013 ;18(12):1285–97.
7. Government of India-- -World Health Organization. Guidelines for Cervical Cancer Screening Programme. 2006 Feb;
8. Mitchell MF, Cantor SB, Brookner C, Utzinger U, Schottenfeld D, Richards-- -Kortum R. Screening for squamous intraepithelial lesions with fluorescence spectroscopy. Obstet Gynecol. 1999 ;94(5, Part 2):889–96.
9. Thekkek N, Richards-- -Kortum R. Optical Imaging for Cervical Cancer Detection: Solutions for a Continuing Global Problem. Nat Rev Cancer. 2008 ;8(9):725–31.
10. Alliance for Cervical Cancer Prevention (ACCP). Planning and implementing cervical cancer prevention and control programs:a manual for managers. Seattle7 ACCP;2004.
11. Winkler J, Bingham A, Coffey P, Penn Handwerker W. Women's participation in a cervical cancer screening program in northern Peru. Health Education Res 2008;23 (1):10-24.
12. Sastri SS, Dinshaw K, Amin G, Goswami S, Patil S, Chinoy R, et al. Concurrent evaluation of Visual, cytological and HPV testing as screening methods for early detection of cervical neoplasia, in Mumbai, India. Bull World Health Organ 2005;83;186-94.
13. Gravitt PE, Paul P, Katki HA, Vendantham H, Ramakrishna G, Sudula M, et al. Effectiveness of VIA, Pap, and HPV DNA testing in a cervical cancer screening program in a peri-urban community in Andhra Pradesh, India. PLoS One. 2010;5(10):e13711.
14. Practice Advisory: Cervical Cancer Screening (Update) - ACOG [Internet]. [cited 2019 Oct 4]. Available from: https://www.acog.org/Clinical-Guidance-and-Publications/Practice-Advisories/Practice-Advisory-Cervical-Cancer-Screening-Update
15. Yousefi Z, Saghafi N, Imannezhad S, Sharifi N, Shirinzadeh L, Rahdari A. The Role of Endocervical Curettage in Satisfactory Colposcopy. Current Women's Health Reviews. 2017 Aug 1;13(2):130-3.
16. Sherigar B, Dalal A, Durdi G, Pujar Y, Dhumale H. Cervical cancer screening by visual inspection with acetic acid - interobserver variability between nurse and physician. Asian Pac J Cancer Prev. 2010;11(2):323-6.
17. Bhatla N, Mukhopadhyay A, Kriplani A, Pandey RM, Gravitt PE, Shah KV, et al. Evaluation of adjunctive tests for cervical cancer screening in low resource settings. Indian J Cancer. 2007;44(2):51-5.
18. Singh A et al. Int J Res Med Sci. 2015 Sep;3(9):2382-2385
19. Gravitt PE, Paul P, Katki HA, Vendantham H, Ramakrishna G, Sudula M, et al. Effectiveness of VIA, Pap, and HPV DNA testing in a cervical cancer screening program in a peri-urban community in Andhra Pradesh, India. PLoS ONE. 2010 Oct 28;5(10):e13711.
20. Concurrent evaluation of visual, cytological and HPV testing as screening methods for the early detection of cervical neoplasia in Mumbai, India. [Internet]. [cited 2019 Oct 4]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2624199/
21. Albert SO, Oguntayo OA, Samaila MOA. Comparative study of visual inspection of the cervix using acetic acid (VIA) and Papanicolaou (Pap) smears for cervical cancer screening [Internet]. 2012 [cited 2019 Oct 1]. Available from: http://ecancer.org/en/journal/article/262-comparative-study-of-visual-inspection-of-the-cervix-using-acetic-acid-via-and-papanicolaou-pap-smears-for-cervical-cancer-screening
22. Asthana S, Labani S, Sodhani P, Gupta S. Co-Testing of Cervical Screening Tests in Detection of High Grade Cervical Intraepithelial Neoplasia. JCDR [Internet]. 2017 [cited 2019 Oct 2]; Available from: http://jcdr.net/article_fulltext.asp?issn=0973-709x&year=2017&volume=11&issue=10&page=XC10&issn=0973-709x&id=10757
23. Shastri SS, Dinshaw K, Amin G, Goswami S, Patil S, Chinoy R, et al. Concurrent evaluation of visual, cytological and HPV testing as screening methods for the early detection of cervical neoplasia in Mumbai, India. Bull World Health Organ. 2005 ;83(3):186–94.