Original Article

Comparison of Visual Inspection Methods with Pap Smear as Screening Test for Premalignant Lesions of the Cervix

Jyoti Yadav, Shubhra Agarwal, Aayushi Jain

Department of Obstetrics and Gynaecology, Teerthanker Mahaveer Medical College and Research Centre, Teerthanker Mahavir University, Moradabad, India

Abstract

Aim and Objectives: The present study was done to compare the visual inspection methods with Pap smear as a screening test for premalignant lesions of the cervix. **Materials and Methods:** The present observational prospective study was done at the Department of Obstetrics and Gynecology at Teerthanker Mahaveer Medical College and Research Center for 18 months. All study subjects were subjected to Papanicolaou smear, VIA, and VILI examination. If any of these tests were found positive, then a colposcopy and cervical biopsy were done. **Results:** The sensitivity of Pap, VIA, VILI, and colposcopy was 52.63%, 84.21%, 73.68%, and 84.21%, respectively. The specificity of Pap, VIA, VILI, and colposcopy was 60.0%, 80.0%, 60.0%, and 80.0%, respectively. The accuracy of Pap, VIA, VILI, and colposcopy was 54.17%, 83.33%, 70.83%, and 83.33%, respectively. **Conclusion:** It is well known that VIA and VILI are very easy to carry out and apply. Even technically they do not cost much, consume less tax and can be applied to all the patients. Even the results are calculated in a faster manner which helps in chalking out the plan in an easy way.

Keywords: *Cervix, colposcopy, Papanicolaou smear, visual inspection of the cervix with acetic acid, visual inspection of the cervix with Lugol's iodine*

Submitted: 09-Oct-2023
Revised: 20-Feb-2024
Accepted: 24-Feb-2024
Published: 04-Apr-2024

Introduction

Cervical cancer ranks second among general malignancies in the reproductive age group in India with more than 1 lakh patients reporting per year.[1] Worldwide, cervical cancer contributes to the major burden in terms of mortality estimated to be around 25%.[2] In low-resource setup countries like ours, it is believed that in the coming decade majority of deaths would be occurring due to cancer cervix.[3]

Cancer cervix consists of a prolonged preinvasive stage that takes approximately 8–10 years to progress into carcinoma. It goes through various stages of cellular atypia, many grades of dysplasia, and then at last invasive cancer.[4] With availability of many screening tests and long pre invasive phase of cervical cancer, it can be prevented through primary prevention. In India, we have existing prevention programs, but still, carcinoma cervix remains the most common factor for mortality and morbidity.[5]

Pap smear is widely used for screening purpose of cervical cancer but it is not cost-effective and requires well-trained staff to collect the samples, well-trained cytopathologist to interpret the samples, making it unsuitable to be used as a screening tool in developing countries.[6]

Visual inspection with acetic acid (VIA) and visual inspection with lugol's iodine (VILI) are simple screening procedure. It is done by naked eye using acetic acid 3-5% and lugol's iodine painting cervical transformation zone. Acetic acid reversibly coagulates nuclear protein leads to white discoloration of transformation zone in cervical intraepithelial neoplasia (CIN) and lugol's iodine shows negative uptake in dysplastic cells due to lack of glycogen. VIA and VILI are cost-effective, give results in the same sitting and treatment can be planned simultaneously.

Address for correspondence: Dr. Aayushi Jain, Sapna Arihant Building, Bastar Road, Dhamtari, Chhattisgarh, India.
E-mail: jaayushi1013@gmail.com

How to cite this article: Yadav J, Agarwal S, Jain A. Comparison of visual inspection methods with Pap smear as screening test for premalignant lesions of the cervix. J Mid-life Health 2024;15:19-24.

Access this article online

Quick Response Code:

Website: https://journals.lww.com/jomh

DOI: 10.4103/jmh.jmh_201_23

Since cervical cancer is preventable and has a longer precancerous stage, its screening is available and can be cured if detected early. There is limited literature with regard to the current topic in the Indian context. The present study was done to compare the visual inspection methods with Pap smear as a screening test for premalignant lesions of the cervix.

Materials and Methods

The present cross-sectional study was done at the Department of Obstetrics and Gynecology at Teerthanker Mahaveer Medical College and Research Center for 18 months after obtaining approval from the ethics committee.

Study population

The study included all sexually active nonpregnant women attending the gynecology outpatient department and admitted to the inpatient department between the age group of 21 and 65 years. The study excluded pregnant females, bleeding per vaginum and active infection, established invasive cervical cancer, iodine allergy, obvious cervical growth, prior treatment for CIN, and women in the puerperium.

Study procedure

A detailed history was obtained from the patient including demographic information such as age, socioeconomic status, education, parity, loss of appetite, age at marriage, age at first coitus, multiple sexual partners, if any combined oral contraceptive (OC) pills use, and complaints such as intermenstrual, postcoital or postmenopausal bleeding, and discharge per vaginum or backache. Pro forma was used to record the information. All study subjects were subjected to Pap smear, VIA, and VILI examination. If any of these tests were found positive, then a colposcopy and cervical biopsy were done.

Data analysis

All information was gathered using a predesigned pro forma and incorporated into the master chart. The statistical analysis was done using the SPSS version 26.0 (SPSS South Asia private limited, Bangalore, Karnataka, India) and appropriate statistical tests were applied. The statistical test used was the Chi-square test.

Results

Out of a total of 19 biopsy-positive cases, Pap smear was positive in 10 (5.26%) cases, whereas 9 cases were false negative. Among five biopsy-negative cases, Pap smear was negative in 3 (60.0%) cases. Two (40.0%) cases were false positive. VIA was positive in 16 (84.2%) cases, whereas amount biopsy-negative cases, VIA was negative in 4 (80.0%) cases. One (20.0%) case was false positive [Tables 1-3].

VILI was positive in 14 (73.7%) cases, whereas among five biopsy-negative cases VILI was negative in 3 (60.0%) cases. Two (40.0%) cases were false positive. Colposcopy was positive in 16 (84.2%) cases, whereas among five biopsy-negative cases colposcopy was negative in 4 (80.0%) cases [Table 4].

Table 1: Demographic distribution of study subjects

	n (%)
Age group (years)	
21–30	65 (24.2)
31–40	96 (35.7)
41–50	79 (29.4)
51–60	27 (10.0)
>60	2 (0.7)
Religion	
Hindu	88 (32.7)
Muslim	181 (67.3)
Socioeconomic status	
Upper class	2 (0.7)
Upper middle	46 (17.1)
Lower middle	8 (3.0)
Upper lower	12 (4.5)
Lower	201 (74.7)

Table 2: Risk factors among the study population

	n (%)
Parity	
Nulliparous	9 (3.3)
1–2	105 (39.0)
3–4	123 (45.7)
≥5	32 (11.9)
Age of first coitus (year)	
15–18	167 (62.1)
19–22	92 (34.2)
23–25	10 (3.7)
Age of first childbirth (years)	
17–20	73 (27.1)
21–24	150 (55.8)
25–27	37 (13.8)
Risk factors	
Smoking	0
Multiparity	260 (96.7)
History of OCP use	42 (15.6)
Poor genital hygiene	213 (79.2)
Symptoms	
Discharge P/V	181 (67.3)
Postcoital bleeding	12 (4.5)
Intermenstrual bleeding	30 (11.2)
Postmenopausal bleeding	5 (1.9)
Low backache	93 (34.6)
Pain lower abdomen	82 (30.5)

OCP: Oral contraceptive pills, P/V: Per vagina

The sensitivity of Pap, VIA, VILI, and colposcopy was 52.63%, 84.21%, 73.68%, and 84.21%, respectively. The specificity of Pap, VIA, VILI, and colposcopy was 60.0%, 80.0%, 60.0%, and 80.0%, respectively. The accuracy of Pap, VIA, VILI, and colposcopy was 54.17%, 83.33%, 70.83%, and 83.33%, respectively [Table 5].

Table 3: Distribution of cases based on Pap smear and HPE findings

	n (%)
Pap smear	
NILM	246 (91.4)
Inflammatory	11 (4.1)
ASC-US	9 (3.3)
LSIL	2 (0.7)
HSIL	1 (0.4)
Malignant cells	0
HPE	
Normal	1 (0.4)
Chronic cervicitis	4 (1.5)
CIN I	16 (5.9)
CIN II	2 (0.7)
CIN III	1 (0.4)
VIA	
Positive	17 (6.3)
VILI	
Positive	16 (5.9)
Colposcopy	
Positive	17 (6.3)

VIA: Vaginal inspection with acetic acid, VILI: Vaginal inspection with Lugol's iodine, HPE: Histopathalogical Examination, CIN: Cervical intraepithelial neoplasia, NILM: Negative for intraepithelial lesion or malignancy, ASC-US: Atypical squamous cell of undetermined significance, LSIL: Low grade squamous intraepithelial lesion, HSIL: High grade squamous intraepithelial lesion

Table 4: Comparison of Pap smear, vaginal inspection with acetic acid, vaginal inspection with Lugol's iodine and colposcopy with biopsy

	Biopsy	
	Positive, *n* (%)	Negative, *n* (%)
Pap smear		
Negative	9 (47.4)	3 (60)
Positive	10 (52.6)	2 (40)
VIA		
Negative	3 (15.8)	4 (80)
Positive	16 (84.2)	1 (20)
VILI		
Negative	5 (26.3)	3 (60)
Positive	14 (73.7)	2 (40)
Colposcopy		
Negative	3 (15.8)	4 (80)
Positive	16 (84.2)	1 (20)

VIA: Vaginal inspection with acetic acid, VILI: Vaginal inspection with Lugol's iodine

Discussion

The malignant lesions in the cervix area are one of the most common forms of genital cancer which are especially observed among Indian women. Even though it is known to all that the rate of mortality as well as morbidity can be reduced by identifying this medical issue during the preinvasive phase of the disease. Even after this, there is no such awareness in India due to the lack of mass screening programs. In a study by Aswathy *et al*.,[7] different sources of information on cervical cancer were identified in which the most common and important source of information mentioned was media followed by health workers, doctors, family and friends.

In our study, there were nonpregnant females in the age group of 21–65 years, most of the participants were below 50 years of age (89%). In study by Possati-Resende *et al*.,[8] the mean age group was 36.9 years. Most of the study females were in the 31-40 age group in present study with median age group resembling closely to Possati-Resende *et al*.[8] Another study by Pankaj *et al*.[9] in Bihar comparing the colposcopy and Pap smear had put the most common age to be between 30 and 40 years.

Our study participants were mainly Muslims and can be a representation of the field practice area of the hospital. Majority of the study participants were from the lower socioeconomic class (74.1%). This finding can also be due to the composition of the serving population by the study hospital; however, socioeconomic class still has a correlation with the cervical cancer as human papillomavirus (HPV) is mostly encountered in females with low-socioeconomic strata also there studies which have shown an increase incidence of cervical cancer in low- and middle-income countries as compared to high-income nations.[10-12] Brackney *et al*.[13] and Jeudin *et al*.[14] in their study also registered similar findings and found that both HPV infection and cervical cancer affect the low-income women and minority women disproportionately, a finding corroborating our present study.

Early age of coitus and or marriage has been shown as an independent risk factor in the causation of cervical cancer.[15-17] Early age of sexual intercourse exposes the vagina to multiple infections coupled with improper hygiene and can result in infection with HPV and subsequent cervical cancer.[17] However, the study in Bangladesh by Nahar *et al*.[18] did not find any significant correlation between the age and incidence of cervical cancer. A meta-analysis by Momenimovahed and Salehiniya[19] clearly stated marriage especially before 16 years of age, a clear risk factor for cervical cancer. In this research, the mean age of marriage of the study

Table 5: Diagnostic value of Pap, vaginal inspection with acetic acid, vaginal inspection with Lugol's iodine and colposcopy

	Pap	VIA	VILI	Colposcopy
Sensitivity (%)	52.63 (28.86–75.55)	84.21 (60.42–96.62)	73.68 (48.8–90.85)	84.21 (60.42–96.62)
Specificity (%)	60.0 (14.66–94.73)	80.0 (28.36–99.49)	60.0 (14.66–94.73)	80.0 (28.36–99.49)
PPV (%)	83.33 (61.17–94.07)	94.12 (73.28–98.94)	87.5 (69.83–95.49)	94.12 (73.28–98.94)
NPV (%)	25.0 (12.38–44.02)	57.14 (30.17–80.45)	37.5 (17.52–62.89)	57.14 (30.17–80.45)
Accuracy (%)	54.17 (32.82–74.45	83.33 (62.62–95.26)	70.83 (48.91–87.38)	83.33 (62.62–95.26)

NPV: Negative predictive value, PPV: Positive predictive value, VIA: Vaginal inspection with acetic acid, VILI: Vaginal inspection with Lugol's iodine

participants was found to be 19.67 ± 2.82 years which is in sync with the scientific facts and findings of the other studies in the past. The mean age of marriage of females in the study by Nessa *et al*.[15] was also 16.3 ± 1 years and the finding is in sync with our present research. Our study also found the age of coitus to be significant with the presence of the cervical premalignant condition, but the age of first childbirth was not significantly associated with the premalignant finding.

As discussed earlier and seen in many studies in the past,[10,11,13] the cervical neoplasm is affected by multiple factors, and the knowledge of these modifiable factors can be beneficial in the prevention of the disease. In our study, we found that most of the subjects came with the risk factor of multiparity (97%) and poor genital hygiene (79%), and a small percentage of females (15.6%) reported a history of OC pill use.

Tufon *et al*.[20] and de Graaff *et al*.[21] also showed a similar result with the risk factor of low age of coitus and multiple sexual partners being the risk factor for the development of disease, the study showed 58.2% of the study participants were OC pill users.

The majority of our patients had vaginal discharge, whereas a significant number of patients had low backache and lower abdominal pain. A very few females reported abnormal bleeding as their symptoms with only five females having postmenopausal bleeding, 12 having postcoital bleeding, and 30 reporting intermenstrual bleeding. The study by Sarkar *et al*.[22] also reported that most of their subjects (87%) presented with excessive, offensive with or without blood-stained vaginal discharge, followed by irregular, heavy, or prolonged vaginal bleeding (61.4%).

The positive predictive value of Pap smear in detecting premalignant conditions was found to be 83.3% with sensitivity and specificity being 52.6% and 60%, respectively. Meanwhile, the negative predictive value (NPV) of Pap was only 25% with an overall accuracy of detecting precancerous lesion of the cervix at 54.2%.

When compared to visual inspection with acetic acid to biopsy, a slightly better result was encountered as VIA had a propensity to detect 16 out of 19 positives and 4 out of 5 negatives with a predictive value of 94%. The accuracy of VIA was 83% with sensitivity and specificity of 84% and 80%, respectively. VIA fared the result similar to colposcopy in every respect.

In the study by Gupta *et al*.,[23] the sensitivity of pap was seen to be 81.4%, specificity of 93.8%, a positive predictive value of 29.6%. Similarly the study outperformed the present research in diagnosis using VIA and VILI with sensitivity and specificity above 85% each method but positive predictive value of less than 16% in both the methods. However Gupta *et al*.[23] considered CIN II as a benchmark of diagnosis while the present research considered pre-malignant lesion as a diagnostic benchmark hence the sensitivity and specificity in the present study is lower as compared to Gupta *et al*.[23] Zahra Vahedpoor *et al*.[24] in their study found that the sensitivity of pap, VIA and a combination of VIA with pap in diagnosis of cervical cancer was 95%, 97% and 30% respectively while the specificity of around 82%, 86% and 71% respectively.

In the study by Khodakarami *et al*.,[25] opinioned indistinguishable manifestations to our present research with the sensitivity, specificity, PPV, NPV, and accuracy of the Pap test and VIA, were 23.5%, 100%, 100%, 86.5% and 87%, 62.5%, 98.8%, 90.9%, 93.2%, and 92.9% respectively. Study done in Kerala by Sankaranarayanan *et al*.[26] found out that sensitivities of low-threshold VIA, high-threshold VIA, VILI, and cytology to detect CIN 2 or worse disease were 88.6%, 82.6%, 87.2%, and 81.9%, respectively; the corresponding specificities were 78.0%, 86.5%, 84.7%, and 87.8%. Fatahi Meybodi *et al*.[27] in their study found a similar range of sensitivity and specificity of colposcopy in the diagnosis of premalignant and cancerous lesion of the cervix, their study revealed that the sensitivity and specificity of colposcopy in the detection of premalignant and malignant cervical lesions were 80.1% and 72.2%, respectively.

In our study, it can be easily inferred that while Pap smear had lower sensitivity and specificity as compared to other methods, VIA fared tremendously better in diagnosing the premalignant lesion, also it was observed that VIA as a method was at par with colposcopy in screening the premalignant condition.

Keeping in view the factors like prevalence of cervical cancer in poor countries like India along with the burden of population, the methods like Pap smear seem outdated as they require a laboratory set up, increase the delay in diagnosis as the patient has to wait for a day or two for the sample to be processed and studied. Similarly, colposcopy also requires a specific skill set with investment in the equipment both of which can be limiting in the resource crunch setting like the Indian subcontinent. However, the Visual Inspection with Acetic acid and Lugol's iodine stands out as an easy and cheaper alternative of colposcopy in the present setting. It has ease of administration with no cumbersome set up with ease of reading the results. It can be done by any trained healthcare worker therefore makes it an ideal screening method for pre-malignant lesion.

The limitation of the current study was that a biopsy was not performed on all cases. Hence, we could not assess the true negative cases. To perform, a biopsy on such a large number is a difficult task, and biopsy being an expensive procedure, poor compliance of participants and increased lost to follow-up were also the contributing factors. Furthermore, studies are still to be done to assess the correct diagnostic value of visual inspection methods in comparison to Pap smear.

Conclusion

In a low-resource country like our visual inspection methods can be considered screening methods as it is well known that VIA and VILI are very easy to carry out and to apply.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, *et al*. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC Cancer Base No. 11. Lyon, France: International Agency for Research on Cancer; 2013.
2. American Cancer Society Published Second Edition of Global Cancer Atlas. Vol. 37. New York: Oncology Times 2015. p. 34.
3. Bhaumik S. India has world's highest number of cervical cancer deaths. BMJ 2013;346:f3108.
4. Smith RA. Expert group: IARC handbooks of cancer prevention. In: Breast Cancer Screening. Vol. 7. Lyon, France: IARC, Breast Cancer Research; 2002-2003. p. 248.
5. Pawaiya AS, Jain I, Juneja K, Dayanithi M, Nagesh S. Self- perceived visual health among women aged 18-59 years in a rural area of Greater Noida, Uttar Pradesh: A cross sectional study. Int J Community Med Public Health 2019;6:2788.
6. Eversole GM, Moriarty AT, Schwartz MR, Clayton AC, Souers R, Fatheree LA, *et al.* Practices of participants in the college of American pathologists interlaboratory comparison program in cervicovaginal cytology, 2006. Arch Pathol Lab Med 2010;134:331-5.
7. Aswathy S, Quereshi MA, Kurian B, Leelamoni K. Cervical cancer screening: Current knowledge and practice among women in a rural population of Kerala, India. Indian J Med Res 2012;136:205-10.
8. Possati-Resende JC, Fregnani JH, Kerr LM, Mauad EC, Longatto-Filho A, Scapulatempo-Neto C. The accuracy of p16/Ki-67 and HPV test in the detection of CIN2/3 in women diagnosed with ASC-US or LSIL. PLoS One 2015;10:e0134445.
9. Pankaj S, Nazneen S, Kumari S, Kumari A, Kumari A, Kumari J, *et al.* Comparison of conventional Pap smear and liquid-based cytology: A study of cervical cancer screening at a tertiary care center in Bihar. Indian J Cancer 2018;55:80-3.
10. Cohen PA, Jhingran A, Oaknin A, Denny L. Cervical cancer. Lancet 2019;393:169-82.
11. Gadelha SR, Soares-Barreto DM, Costa GB, Leal VC, Gomes LG, Santos UR, *et al.* Clinical, laboratory and epidemiological aspects of HPV infection in a low-income population from South Bahia, Brazil. Epidemiol Infect 2017;145:3398-404.
12. Bhatta MP, Johnson DC, Lama M, Aryal S, Lhaki P, Shrestha S. High-risk human papillomavirus infection and abnormal cervical cytology among Nepali and Bhutanese refugee women living in Eastern Nepal. BMC Infect Dis 2017;17:73.
13. Brackney MM, Gargano JW, Hannagan SE, Meek J, Querec TD, Niccolai LM. Human papillomavirus 16/18-associated cervical lesions: Differences by area-based measures of race and poverty. Am J Prev Med 2020;58:e149-57.
14. Jeudin P, Liveright E, Del Carmen MG, Perkins RB. Race, ethnicity, and income factors impacting human papillomavirus vaccination rates. Clin Ther 2014;36:24-37.
15. Nessa A, Ara R, Fatema P, Nasrin B, Chowdhury A, Khan KH, *et al.* Influence of demographic and reproductive factors on cervical pre-cancer and cancer in Bangladesh. Asian Pac J Cancer Prev 2020;21:1883-9.
16. Sreedevi A, Javed R, Dinesh A. Epidemiology of cervical cancer with special focus on India. Int J Womens Health 2015;7:405-14.
17. Kashyap N, Krishnan N, Kaur S, Ghai S. Risk factors of cervical cancer: A case-control study. Asia Pac J Oncol Nurs 2019;6:308-14.
18. Nahar Q, Sultana F, Alam A, Islam JY, Rahman M, Khatun F, *et al.* Genital human papillomavirus infection among women in Bangladesh: Findings from a population-based survey. PLoS One 2014;9:e107675.
19. Momenimovahed Z, Salehiniya H. Cervical cancer in Iran: Integrative insights of epidemiological analysis. Biomedicine (Taipei) 2018;8:18.
20. Tufon EN, Yuwun Novert B, Egba S, Ndohnui NN. Prevalence, associated risk factors and methods of diagnosing cervical cancer in two hospitals in Yaounde, Cameroon. Int J Adv Res Pharma Bio Sci 2011.

21. de Graaff J, Stolte LA, Janssens J. Marriage and childbearing in relation to cervical cancer. Eur J Obstet Gynecol Reprod Biol 1977;7:307-12.
22. Sarkar M, Konar H, Raut D. Symptomatology of gynecological malignancies: Experiences in the gynecology out-patient clinic of a tertiary care hospital in kolkata, India. Asian Pac J Cancer Prev 2010;11:785-91.
23. Gupta S, Kyal A, Mukhopadhyay P. Visual inspection methods as screening test for cervical cancer in low – Resource settings. J South Asian Feder Obst Gynae 2018;10:88-91.
24. Vahedpoor Z, Behrashi M, Khamehchian T, Abedzadeh-Kalahroudi M, Moravveji A, Mohmadi-Kartalayi M. Comparison of the diagnostic value of the visual inspection with acetic acid (VIA) and pap smear in cervical cancer screening. Taiwan J Obstet Gynecol 2019;58:345-8.
25. Khodakarami N, Farzaneh F, Aslani F, Alizadeh K. Comparison of pap smear, visual inspection with acetic acid, and digital cervicography as cervical screening strategies. Arch Gynecol Obstet 2011;284:1247-52.
26. Sankaranarayanan R, Wesley R, Thara S, Dhakad N, Chandralekha B, Sebastian P, *et al.* Test characteristics of visual inspection with 4% acetic acid (VIA) and Lugol's iodine (VILI) in cervical cancer screening in Kerala, India. Int J Cancer 2003;106:404-8.
27. Fatahi Meybodi N, Karimi-Zarchi M, Allahqoli L, Sekhavat L, Gitas G, Rahmani A, *et al.* Accuracy of the triple test versus colposcopy for the diagnosis of premalignant and malignant cervical lesions. Asian Pac J Cancer Prev 2020;21:3501-7.