

DOI: <https://dx.doi.org/10.18203/2320-1770.ijrcog20242069>

Original Research Article

The study of diagnostic value of pap smear comparing with visual inspection of cervix after acetic acid application in detecting premalignant lesions of cervix

Shubhangi A. Bedekar*, Girish B. Karmarkar, Pranali Diwadkar

Department of Obstetrics and Gynecology, Parkar Hospital, Ratnagiri, Maharashtra, India

Received: 03 May 2024

Revised: 09 July 2024

Accepted: 10 July 2024

*Correspondence:

Dr. Shubhangi A. Bedekar,

E-mail: shubhangib88@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Objective of the study was to compare the effectiveness of VIA and pap smear for screening of premalignant lesions of cervix and to compare the performance of VIA used alone and combined with pap smear for screening of premalignant lesions of cervix.

Methods: VIA and Pap smear were performed in 260 patients attending routine gynaecology OPD. Positive cases of either or both screening tests were subjected to colposcopy and biopsy if indicated. The reports of histopathology were correlated with the pap smear and VIA findings and thereby sensitivity, specificity, positive and negative predictive values of each of the screening methods were calculated and results were analysed.

Results: 260 patients were screened for premalignant lesions of cervix by VIA and pap smear both, 37 of 260 patients, (14.2%) were VIA positive, 30 of 260 patients (11.5%) were pap smear positive, 20 of 260 patients (7.69%) were positive for VIA as well as pap smear, 25 of 260 patients (9.6%) were confirmed of premalignant lesions on histopathology, 24 patients were diagnosed CIN and one patient was diagnosed with CIS.

Conclusions: VIA has lower sensitivity and specificity compared to Pap smear but the results are comparable. Both the tests are fairly accurate. A combination of VIA and Pap smear increased the sensitivity and specificity to 100%.

Keywords: Cervical cancer screening, Pap smear, VIA

INTRODUCTION

Cervical cancer is a leading malignancy worldwide. It is the 2nd most common cancer in females after breast. Cancer cervix is also the 4th most common cancer-causing death. About 662,301 new cervical cancer cases are diagnosed annually in the World.³In India, cervical cancer is the 2nd most common cancer in females accounting for 22.86% of all cancer cases in women and 12% of all the cancer cases in both males and females.¹ Annual crude incidence rate per 100,000 (World): 15.8. Annual crude mortality rate per 100,000 (World): 8.84.^{1,3} Cervical cancer is a preventable disease as it has a long preinvasive

stage, cervical cytology screening programs are currently available and the treatment of preinvasive lesions is effective. It has been well established that well organised screening by cytology has substantially reduced the incidence of morbidity and mortality of cervical cancer in developed countries. It is apparent that a current problem facing the developing world is a lack of cervical cancer screening. Women in resource limited areas often have higher exposure to cervical cancer risk factors including multiple sexual partners, poverty, multi-parity, tobacco use, malnutrition, and poor genital hygiene. This brings into sharp focus the need to implement the tools already available for cervical cancer prevention and treatment. The

currently available screening methods are conventional cytology, liquid-based cytology, visual inspection of acetic acid (VIA), visual inspection of Lugol's iodine (VILI), HPV DNA testing and colposcopy. Various developed countries have institutionalized Pap cytology test or HPV DNA as primary method of screening, which is time consuming, expensive, require advance infrastructure and are not widely available. Common problems encountered with colposcopy are inadequate expertise, interpretation difficulties, disagreements, and failure to follow standard diagnostic protocol. Conventional cytology is a safe, inexpensive, non-invasive and effective method for detecting precancerous lesions of cervix. However, it also requires laboratory facilities and pathologist.²⁻⁶ VIA and VILI are again safe, inexpensive, simple administration and provide quick results and closely match pap smear in its performance in detecting cervical cancer precursors. The significantly limited impact of cytology based cervical cancer screening programs in developing countries is now widely recognized. There are several reasons for these limits, ranging from the nature of participation of women in screening programs to the access and timely completion of treatment when necessary. Cytology laboratories are expensive to maintain and there are often delays before the results become available, leading to issues with follow up when transportation difficulties exist.⁹

Non-cytologic tests, such as visual inspection of the cervix with acetic acid (VIA) avoid reliance on expensive laboratory equipment and overcome other recognized barriers. Common household vinegar applied on the cervix will cause areas of dysplasia to appear bright white. This screening test can be performed at the bedside by a range of trained providers including physicians, nurses, and nurse-midwives, and has been shown to be safe and efficacious. The ability to obtain instantaneous results allows for immediate treatment and reduces loss to follow-up.⁸ Screening with VIA has been shown to be effective in low resource settings at decreasing the prevalence of high-grade precursor lesions and the low cost and simplicity of the procedure affirm its aptitude as an initial screening tool.^{9,16} In this background of limited studies about comparison between pap smear and VIA in the north Indian population, the study was conducted to compare the efficacy between the two screening methods- Pap smear and VIA.

METHODS

The study was conducted in the Obstetrics and Gynaecology department of Government Multi speciality Hospital, Sector 16, Chandigarh between the period of March 2016 to December 2017. After fulfilling the inclusion and exclusion criteria patients attending routine gynaecology OPD were recruited in the study. Written informed valid consent was obtained from each woman willing to participate in the study. Relevant socio demographic, obstetric and gynaecological history was also obtained through a questionnaire. Medical officers and resident doctors from the department of obstetrics and

gynaecology performed clinical examination of the subjects. Of which pap smear was done and cervical examination done with acetic acid. A PAP test of Atypical Squamous Cells of Undetermined Significance and above were considered as positive. A positive VIA result implied definite acetowhite areas (dense, opaque, sharp, distinct, rapidly arriving and lasting long with or without raised margins) touching the squamocolumnar junction. Positive cases of either or both screening tests were subjected to colposcopy. Patients were referred for colposcopy to the PGIMER. Samples for histopathology were obtained by colposcopy guided biopsy as clinically indicated. The reference standard for defining final disease status was a combination of colposcopy and biopsy. Disease status was assessed on the basis of histology if a biopsy was taken; if not, on the basis of colposcopy. Reference standard negatives included women who were assessed as normal by colposcopy, as well as those who were assessed as positive by colposcopy, but negative by histology. The reports of histopathology were correlated with the pap smear and VIA findings and thereby sensitivity, specificity, positive and negative predictive values of each of the screening methods were calculated and results were analysed.

RESULTS

The age of the women recruited in the study ranged between 25 to 60 years. The mean age of the women in the study was 41.07 ± 7.59 years. The Figure 1 depicts proportion of women in our study according to age majority of women i.e. 109 (41.9%) were between the age group of 41-50 years.

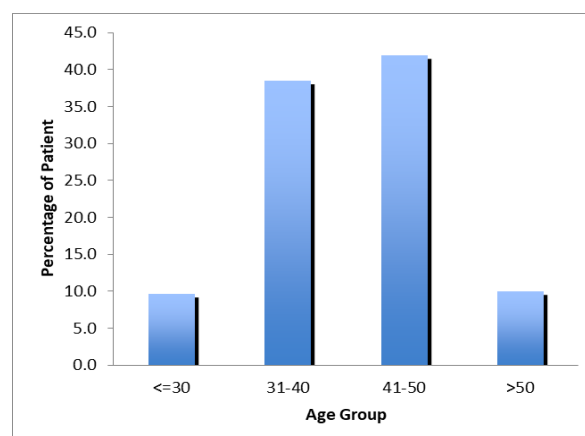


Figure 1: Age distribution of the study population.

Figure 2 depicts the distribution of years of married life in the study population. Mean years of married life is 21.66 ± 8.90 years.

The Figure 3 depicts the proportion of literacy among the women in our study group. Among all the subjects, 24% women were illiterate rest 76% had received formal school education.

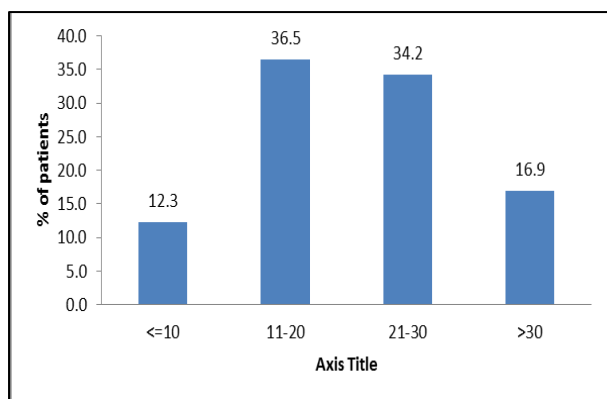


Figure 2: Years of married life.

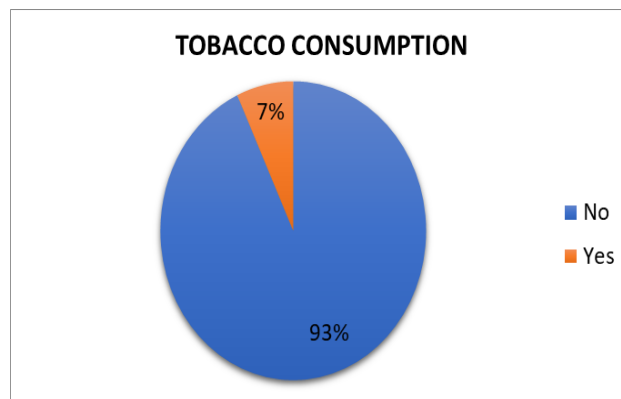


Figure 5: Tobacco consumption.

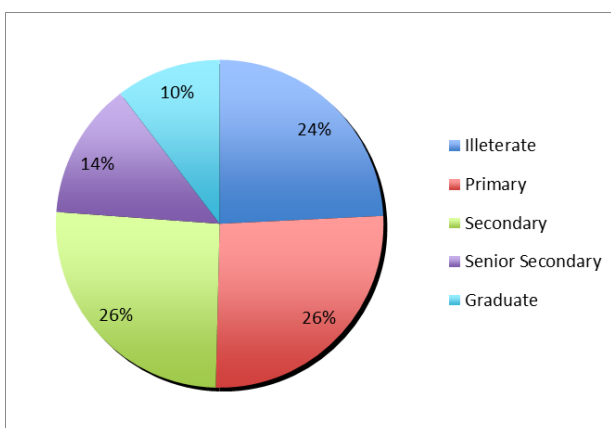


Figure 3: Education.

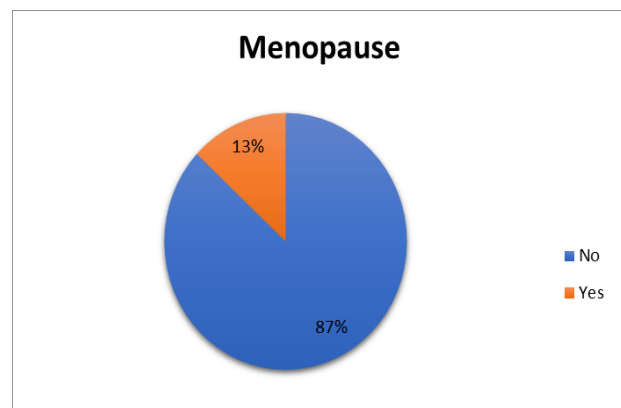


Figure 6: Menopause.

Figure 6 shows the proportion of premenopausal and postmenopausal women in our study. Around 13% of women were postmenopausal and 87% women were premenopausal.

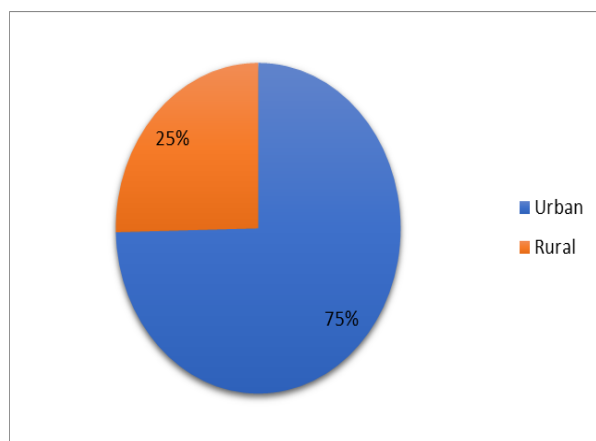


Figure 4: Residence.

Figure 4 depicts the proportion of women staying in urban and rural areas. 74.6% of the study population lived in the urban area and the remaining 25.4% stayed in the rural area.

Figure 5 depicts the proportion of tobacco consumers in the population. 7 % of the study population was tobacco consumer while remaining 93% was not a consumer of tobacco.

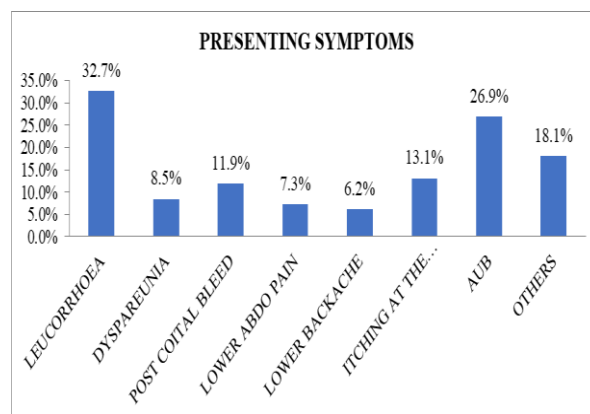


Figure 7: Presenting symptoms.

There were three babies who developed respiratory 260 patients were screened for premalignant lesions of cervix by VIA and pap smear both, 37 of 260 patients (14.2%) were VIA positive, 30 of 260 patients (11.5%) were pap smear positive, 20 of 260 patients (7.69%) were positive for VIA as well as pap smear.

Table 1: Results of the screening tests.

	Frequency	Percentage
Via	37/260	14.2
Pap smear	30/260	11.5
Histopathology	25/260	9.6

A total 25 of 260 patients (9.6%) were confirmed of premalignant lesions on histopathology, 24 patients were diagnosed CIN and one patient was diagnosed with CIS. Most common presenting complaint seen in patients with positive VIA cases was observed to be post coital bleed accounting for 43.2 % of the positive cases whereas with positive cytology cases was observed to be post coital bleed accounting for 50 % of the positive cases. Out of the 37 VIA positive cases: 22 were true positive for premalignant lesions of cervix. 15 were diagnosed negative on histopathology of the 22 diagnosed premalignant lesions, 14 were CIN 1, 6 were CIN 2, 1 was CIN 3, 1 was CIS. 3 cases diagnosed CIN positive on histopathology were missed by VIA. All the three cases missed by VIA were CIN 1. No case of CIN 2 and above was missed by VIA. Out of the 30 cases diagnosed positive on Pap smear: 26 were ASCUS positive, 4 were LSIL positive. 7 ASCUS positive were detected to be chronic cervicitis/ normal on histopathology, 19 ASCUS positive cases were detected to be premalignant on histopathology: 15 were diagnosed CIN 1, 4 were diagnosed CIN 2. Out of the 4 LSIL cases 2 were diagnosed CIN 2, 1 was diagnosed CIN 3, 1 was detected CIS on histopathology. 2 cases of CIN 1 were missed by Pap smear. No case of CIN 2 and above were missed by Pap smear. In 20 patients wherein both the screening tests were positive histopathology confirmed premalignant lesions in all of them, 8 with CIN 1, 6 with CIN 2, 1 with CIN 3, 1 with CIS.

Table 2: Test characteristics of screening tests.

Tests	VIA	Pap smear	Combined screening
Diagnostic Accuracy	93.1%	96.5	100
Sensitivity	88.0%	92	100
Specificity	93.6%	97	100
Positive Predictive Value	59.5%	76.7	100
Negative Predictive Value	98.7%	99.1	100

DISCUSSION

The sensitivity of VIA in our study was 88% which was comparable to David et al (94.7%), Vahedpoor et al (94.6%) and Sinha et al (93.3%), Harsono et al (80%), Shreshtha et al (81.25%).^{12,14,17,18} The specificity of VIA in our study was 92%. The result was comparable to many of the previous studies like Harsono et al (96.4%), David et al (88%), Banerjee et al (92%), Shriniwas et al (86%).^{12,17,24} The sensitivity of Pap smear in our study was

92%. It was slightly higher than many of the previous studies. David et al (89.5%), Lagos castillo et al (87%), Shreshtha et al (100%), Shrivastava et al (94%), Sinha et al (93.8%) had a comparable sensitivity to our result.^{12,13,26} The reason for higher sensitivity of Pap smear in our study could be that ASCUS was used as cut off for positive cases whereas most other studies used LSIL as a cut off. The specificity of Pap smear in our study was 97%. The result was like previous studies like Smith et al (97.4%), Goel et al (97%), Bathla et al (98.9%), Hegde et al (98%), Chouhan et al (93.5%), Shreshtha et al (91.3%), Nayak et al (94.3%), Banerjee et al (95%), Lagos Castello et al (100%).^{8,9,11-13,19-21,26} As mentioned in the table above, most of the previous studies suggest that VIA was more sensitive and less specific than Pap smear. The results of the current study suggests that VIA was less sensitive and less specific than Pap smear. These results were consistent with Sankara Narayan et al Hegde et al Consul et al.^{19,20,25} Verification bias is a phenomenon in which only the screen positive subjects get an opportunity to be subjected to the accepted gold standard (colposcopy- in this study).

The PPV of VIA and Pap smear in our study were 59.5 and 76.7. Similar results were also observed in other studies like David et al, Mremi et al, Lagos castillo et al, Nayak et al, Shreshtha et al, Vahedpoor et al.^{4,12,13,15,18,26} The NPV in our study was 98.7 for VIA and 99.1 for Pap smear. The results were consistent with the studies of David et al, Mremi et al, Lagos castillo et al, Nayak et al, Shreshtha et al, Vahedpoor et al.^{4,12,13,16,18,26} In a meta-analysis done by Fahey et al in 1995 involving 62 studies conducted between 1984 and 1992, the mean sensitivity and specificity of cytology was 58% (range 11-99%) and 68% (range 14-97%), respectively.²³ In another recent meta-analysis by Nanda et al in 2000 the sensitivity of cytology to the detection of CIN 2 or worse lesions ranged from 18% to 98% and the specificity ranged from 17% to 99%.²⁴ In the IARC multicentre study done by Sankaranarayanan et al the Pap smear showed lowest sensitivity, even at the lowest cut off ASCUS (57%; 95% CI 38-76%) for CIN2 + but the specificity was rather high (93%; 95% CI 89-97%).²⁰ The reason behind such a wide variation in these results could be that their study excluded verification bias and the cut off for histology to be considered positive was CIN 2+ whereas the present study did not exclude verification bias and considered CIN 1 as a cut off for histology. A combination of inputs in training, and quality control and evaluation of cytology results by the same cytopathologists seems to be responsible for the satisfactory performance of cytology in our study. In the IARC multicentre study done in India and Africa by Sankaranarayanan et al in 2004 which included 11 cross-sectional studies, the sensitivity of VIA ranged from 56.10% to 93.90% and the specificity ranged between 74.20% and 93.80%.²⁷ The large variation in these results indicates that several variables affect the test characteristics of visual inspection with acetic acid which are lack of standard criteria for test positivity, inter-observer variation, light source, presence of co-existing infection, inflammation, and metaplasia.

The sensitivity, specificity, PPV and NPV were 100% each when both the screening methods were used simultaneously. Thereby markedly improving the performance of each of them singly. This study was a single-centered study; thus, its results cannot be applicable to all populations. Also, the sample size was small and hence similar study with a bigger sample size needs to consolidate the results.

CONCLUSION

As per the results of our study, VIA has lower sensitivity and specificity compared to Pap smear but the results are comparable. Both the tests are fairly accurate. A combination of VIA and Pap smear increased the sensitivity and specificity to 100%. Replacing conventional cytology by VIA is not recommended however VIA is a promising alternative not only in low resource settings where access to cytology-based screening programmes is unavailable but also in well-equipped centres. Pap smear can be used for further diagnosis. However, biopsy is confirmative. The advantage with VIA is that it is inexpensive, requires minimum resources that are locally available can be performed by paramedical staff when provided with training and results are immediately available thereby reducing the anxiety of the patient involved in waiting time for the cytology report. In developing countries most of the women who undergo screening with Pap smear do not come for follow up or do not collect their report on time thereby leading to delay in diagnosis and management and at times, missing the cases. In conclusion, in low resource settings, screening of carcinoma cervix by Pap smear can be replaced by cheaper and easily available visual methods like VIA, which has the high sensitivity to detect dysplasia, with a reasonable specificity. Even when screening with Pap smear is available, it should be combined with VIA, as cases of CIN missed by Pap smear were picked up by the VIA.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Bruni L, Albero G, Serrano B, Mena M, Collado JJ, Gómez D. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). Human Papillomavirus and Related Diseases in the World. Summary Report; 2023.
2. Krishnamurthy A, Ramshankar V. Current Status and Future Perspectives of Molecular Prevention Strategies for Cervical Cancers. *Indian J Surg Oncol.* 2020;11(4):752-61.
3. Ferlay J, Ervik M, Lam F, Laversanne M, Colombet M, Mery L. Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer; 2024.
4. Mremi A, Mchome B, Mlay J, Schledermann D, Blaakær J, Rasch V. Performance of HPV testing, Pap smear and VIA in women attending cervical cancer screening in Kilimanjaro region, Northern Tanzania: a cross-sectional study nested in a cohort. *BMJ Open.* 2022;12(10):64321.
5. Chouhan AS, Prinja S, Srinivasan R, Rai B, Malliga JS, Jyani G et al. Cost effectiveness of strategies for cervical cancer prevention in India. *PLoS One.* 2020;15(9):23829.
6. Srivastava AN, Misra JS, Srivastava S, Das BC, Gupta S. Cervical cancer screening in rural India: Status & current concepts. *Indian J Med Res.* 2018;148(6):687-96.
7. Sharma J, Yennapu M, Priyanka Y. Screening Guidelines and Programs for Cervical Cancer Control in Countries of Different Economic Groups: A Narrative Review. *Cureus.* 2023;15(6):41098.
8. Slavkovsky RC, Bansil P, Sandoval MA, Figueroa J, Rodriguez DM, Lobo JS. Health outcomes at 1 year after thermal ablation for cervical precancer among human papillomavirus- and visual inspection with acetic acid-positive women in honduras. *JCO Glob Oncol.* 2020;6:1565-73.
9. Screening and management of preinvasive lesions of the cervix: good clinical practice recommendations from the Federation of Obstetrics and Gynaecologic Societies of India (FOGSI) Bhatla N, Singhal S, Saraiya U, et al. *J Obstet Gynaecol Res.* 2020;46:201–14.
10. Hon HJ, Chong PP, Choo HL, Khine PP. A Comprehensive Review of Cervical Cancer Screening Devices: The Pros and the Cons. *Asian Pac J Cancer Prev.* 2023;24(7):2207-15.
11. Smith SK, Nwosu O, Edwards A, Zerihun M, Chung MH, Suvada K et al. Performance of screening tools for cervical neoplasia among women in low- and middle-income countries: A systematic review and meta-analysis. *PLOS Glob Public Health.* 2023;3(2):1598.
12. David J, Joshi V, Jebin Aaron D, Baghel P. A comparative analysis of visual inspection with acetic acid, cervical cytology, and histopathology in the screening and early detection of premalignant and malignant lesions of the cervix. *Cureus.* 2022;14(9):29762.
13. Shrestha AD, Andersen JG, Gyawali B, Shrestha A, Shrestha S, Neupane D. Cervical cancer screening utilization, and associated factors, in Nepal: a systematic review and meta-analysis. *Public Health.* 2022;210:16-25.
14. Kangethe JM, Monroe-Wise A, Muiruri PN, Komu JG, Mutai KK, Nzivo MM. Utilisation of cervical cancer screening among women living with HIV at Kenya's national referral hospital. *South Afr J HIV Med.* 2022;23(1):1353.
15. Nayak PK, Mitra S, Agrawal S, Hussain N, Thakur P, Mishra B. Role of various screening techniques in detecting preinvasive lesions of the cervix among

- symptomatic women and women having unhealthy cervix. *J Cancer Res Ther.* 2021;17(1):180-5.
16. Shrestha B, Malla Vaidya K, Joshi R. Evaluation of Visual Inspection of Cervix with Acetic Acid and Liquid Based in Cervical Cancer Screening with Cervical Biopsy. *J Nepal Health Res Counc.* 2020;18(3):426-30.
 17. Harsono AB, Susiarno H, Suardi D, Owen L, Fauzi H, Kireina J. Cervical pre-cancerous lesion detection: development of smartphone-based VIA application using artificial intelligence. *BMC Res Notes.* 2022;15(1):356.
 18. Vahedpoor Z, Behrashi M, Khomehchian 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(3):345-8.
 19. Screening for cancer in low- and middle-income countries. Sankaranarayanan R. *Ann Glob Health.* 2014;80:412-7.
 20. Hegde D, Shetty H, Shetty PK, Rai S. Diagnostic value of acetic acid comparing with conventional pap smear in the detection of colposcopic biopsy-proved CIN *J Cancer Res Ther.* 2011;7:454-8.
 21. Goel A, Gandhi G, Batra S, Bhambhani S, Zutshi V, Sachdeva P. Visual inspection of the cervix with acetic acid for cervical intraepithelial lesions *Int J Gynaecol Obstet.* 2005;88:25-30.
 22. Fahey MT et al. Meta-analysis of Pap test accuracy. *American Journal of Epidemiology.* 1995;141:680-9.
 23. Nanda K. Accuracy of the Papanicolaou test in screening for and follow-up of cervical cytologic abnormalities: a systematic review. *Annals of Internal Medicine.* 2000;132:810-9.
 24. Srinivas V, Nishimura HM, Jayakrishna P, Krupp K, Madhivanan P, Madhunapantula SV. Evaluating the feasibility of utilizing Gynocular-triage-to-diagnose application with VIA (Visual inspection with Acetic acid) in community cervical cancer screening programs in rural Mysore, India. *Indian J Cancer.* 2021;58(3):409-16.
 25. Consul S, Agrawal A, Sharma H, Bansal A, Gutch M, Jain N. Comparative study of effectiveness of pap smear versus visual inspection with acetic acid and visual inspection with lugol's iodine for mass screening of premalignant and malignant lesion of cervix *Indian J Med Paediatr Oncol.* 2012;33:161-5.
 26. Lagos-Castillo M, Guevara-Vizcarra M, Paredes-Campos F, Kosuri S, Vilchez G. The effectiveness of pap and visual inspection with acetic acid (via) tests in cervical dysplasia screenings during the COVID-19 pandemic. *Cureus.* 2022;14(7):27364.
 27. Sankaranarayanan R, Basu P, Wesley RS, Mahe C, Keita N, Mbalawa CC. IARC multicentre study group on cervical cancer early detection. accuracy of visual screening for cervical neoplasia: Results from an IARC multicentre study in India and Africa. *Int J Cancer.* 2004;110(6):907-13.

Cite this article as: Bedekar SA, Karmarkar BG, Diwadkar P. The study of diagnostic value of pap smear comparing with visual inspection of cervix after acetic acid application in detecting premalignant lesions of cervix. *Int J Reprod Contracept Obstet Gynecol* 2024;13:2050-5.