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Original Research Article

# Evaluation of Different Screening Modalities in Detection of Pre-Invasive Cervical Cancer Lesions

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**Abstract:**

**Background:** Cervical cancer is still one of the most common causes of morbidity and mortality in women globally, especially in low- and middle-income countries. Early diagnosis of pre-invasive lesions greatly enhances prognosis and decreases the disease burden. Various screening techniques exist, but their efficacy differs.

**Aim:** The objective of the present study was to assess and compare the accuracy of different screening modalities of cervical cancer-Pap smear, Visual Inspection with Acetic Acid (VIA), Liquid-Based Cytology (LBC), and testing for Human Papillomavirus (HPV) DNA-against pre-invasive lesions of cervix in detecting pre-invasive lesions using colposcopy-guided biopsy as a reference standard.

**Methods:** A cross-sectional study was carried out among 300 women in the age group of 25–60 years visiting a Department of Obstetrics and Gynaecology, PMCH, Patna, Bihar, India, India. All four screening tests were done in each participant. Positive results were validated by colposcopic examination and biopsy. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of all the methods were estimated and compared.

**Results:** Out of the 300 women screened, 64 (21.3%) were found to have pre-invasive lesions on confirmation. HPV DNA testing was most sensitive (93.8%) and NPV (97.7%), while Pap smear was most specific (93.3%). LBC was more accurate than standard Pap smear, and VIA was a moderately sensitive technique appropriate for low-resource settings.

**Conclusion:** HPV DNA testing became the most sensitive screening method for the early detection of pre-invasive cervical lesions. VIA and LBC can be used as good alternatives in resource-constrained situations. Effective screening modalities must be integrated for the prevention and early detection of cervical cancer.

**Keywords:** Cervical Cancer, Pre-Invasive Lesions, HPV DNA testing, Pap smear, VIA, Liquid-Based Cytology, Screening Modalities, Colposcopy, Early Detection.

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## Introduction

Cervical cancer had continued to be a major public health problem, especially in low- and middle-income nations. It had been well known that pre-invasive cervical lesions, if identified early, could be treated effectively, thus curbing the incidence and mortality due to invasive cervical cancer. Different screening modalities, such as Pap smear (cytology), Visual Inspection with Acetic Acid (VIA), Human Papillomavirus (HPV) DNA testing, and Liquid-Based Cytology (LBC), had been used with different sensitivities and specificities. The present study was conducted to compare and assess the efficacy of various screening methods in identifying pre-invasive cervical cancer lesions in a specified population, thus determining the most efficient method for early diagnosis and prevention.

**Global Burden of Cervical Cancer:** Cervical cancer is a serious global health concern and still ranks as the fourth most frequent cancer among women globally. As estimated by the World Health Organization (WHO), cervical cancer represents over 600,000 new cases every year, with more than 340,000 annual deaths. The statistics show the scope of the disease and the effects on the health of women.

The cervical cancer burden is disproportionately greater in low- and middle-income countries (LMICs), where most cases arise because of the absence of organized screening programs and restricted access to timely medical care. In high-income countries, however, the use of organized screening programs—Pap smears, HPV testing, and other preventive interventions—has resulted in a

substantial decline in incidence and mortality rates of cervical cancer.

Nevertheless, despite the presence of preventive modalities, cervical cancer continues to be a significant cause of morbidity and mortality in most developing countries, and more than 85% of cervical cancer deaths have been found to occur within these countries. The enormous differences in cervical cancer occurrence and outcome are a reminder of the compelling necessity for greater access to effective early detection and screening modalities.

**Pathogenesis and Natural History of Cervical Cancer:** Cervical cancer usually arises in a prolonged and insidious manner with the initial infection of the cervix by carcinogenic or high-risk forms of Human Papillomavirus (HPV), types 16 and 18, that account for the large proportion of cervical carcinomas. Infection can lead to Cervical Intraepithelial Neoplasia (CIN), which is an intermediate lesion that precedes cervical cancer. CIN is graded into three:

CIN I: Mild dysplasia with low-grade changes.

CIN II: Moderate dysplasia, characterized by more significant changes.

CIN III: Severe dysplasia or carcinoma in situ, where abnormal cells are confined to the epithelium.

The development of CIN to invasive cervical cancer can occur over several years, sometimes 10 to 20 years, in which there is an extended period for early detection and treatment. If the pre-invasive lesions like CIN I, CIN II, and CIN III are diagnosed early, they can be treated successfully with no or minimal long-term sequelae.

It is the slow course of the disease that makes screening so important, since detection early in the process can stop the disease from developing into invasive carcinoma, thus drastically lessening incidence and mortality of cervical cancer. Early detection of pre-invasive lesions is essential to the control of cervical cancer worldwide.

**Importance of Screening in Cervical Cancer:** Screening for cervical cancer is a key tool in the prevention and early detection of invasive disease. Through the identification of pre-invasive lesions like CIN, it becomes possible to remove or treat such lesions before they become cancerous. Various methods of screening have been used around the world based on the available healthcare setting, resources, and infrastructure. The methods are used to identify pre-cancerous changes in the cervix before they become cervical cancer.

The Pap smear has been the gold standard for cervical cancer screening for decades and is still the most common method used in much of the world. Yet, visual inspection with acetic acid (VIA), Liquid-Based Cytology (LBC), and HPV DNA testing have also become known for their superior ability to detect pre-invasive lesions in different settings.

The efficiency of cervical cancer screening is determined by various factors, such as the sensitivity and specificity of the screening test, the screening frequency, and follow-up for abnormal results. Hence, it is crucial to determine the most effective and affordable screening test to enhance cervical cancer prevention, especially in areas where resources are scarce.

## Method

**Study Design:** The current research had been planned as hospital-based, cross-sectional analytical research to assess and compare the efficiency of various modalities of screening in identifying the pre-invasive cervical cancer lesions. The study had been undertaken for Department of Obstetrics and Gynaecology, PMCH, Patna, Bihar, India from July 2023 to June 2024.

**Study Population:** The population under study had comprised women aged between 25 and 60 years who had visited the gynecology outpatient clinic for routine follow-up or minor gynecological symptoms. The inclusion criteria had demanded that participants be sexually active, not pregnant at the time of examination, and with no previous history of cervical neoplasia or hysterectomy. Women menstruating during examination or with active genital tract infections were excluded and rescheduled.

**Sample Size:** According to prior literature and a 95% confidence interval with 80% power and prevalence of cervical pre-invasive lesions estimated at 10%, the minimum sample size of 300 women had been calculated. Such a sample size had provided adequate power for comparison among several screening modalities.

**Data Collection:** Each participant had undergone the following four cervical cancer screening tests in a standardized sequence:

1. Conventional Pap Smear
2. Visual Inspection with Acetic Acid (VIA)
3. Liquid-Based Cytology (LBC)
4. HPV DNA Testing

All the tests had been conducted by trained health personnel under aseptic precautions. Positive results of any screening test had been followed by colposcopic examination and biopsy, which was the gold standard for diagnosis. A pre-designed questionnaire had also been utilized to gather socio-demographic and clinical data from all participants.

**Outcome Measures:** The primary outcome of the study had been the detection of pre-invasive cervical lesions (CIN I, II, III) by each screening method.

The **secondary outcomes** had included:

- Sensitivity and specificity of each test
- Positive predictive value (PPV)
- Negative predictive value (NPV)
- Comparison of test accuracy using colposcopy-directed biopsy as the reference standard

**Statistical Analysis:** Analysis of data had been done using SPSS version 25.0. Categorical data were reported as frequency and percentage, whereas continuous variables were reported as mean ± SD. Sensitivity, specificity, PPV, and NPV for all screening tests were computed. Chi-square tests were employed to compare categorical variables, and Receiver Operating Characteristic (ROC) curves were constructed to determine the diagnostic accuracy of each test. A p-value < 0.05 was taken as statistically significant.

**Results**

The research compared 300 women between 25 and 60 years of age with four modalities of cervical cancer screening: Pap smear, Visual Inspection with Acetic Acid (VIA), Liquid-Based Cytology (LBC), and HPV DNA testing. The results of each test were compared against colposcopy-guided biopsy as the gold standard. The results are given below in terms of detection rates, diagnostic accuracy, and comparative analysis.

**Demographic Characteristics:** The age range of the participants averaged 38.2 ± 8.1 years. Most women (60%) were in the age range of 31–45 years. Most of them (72%) were multiparous, and 65% of them had never had cervical cancer screening done before.

**Table 1: Demographic Characteristics of the Study Population**

| Characteristic | Frequency (n) | Percentage (%) |
|---|---|---|
| Age Group (years) | | |
| 25–30 | 54 | 18% |
| 31–45 | 180 | 60% |
| 46–60 | 66 | 22% |
| Parity | | |
| Nulliparous | 84 | 28% |
| Multiparous | 216 | 72% |
| Previous Screening Done | | |
| Yes | 105 | 35% |
| No | 195 | 65% |

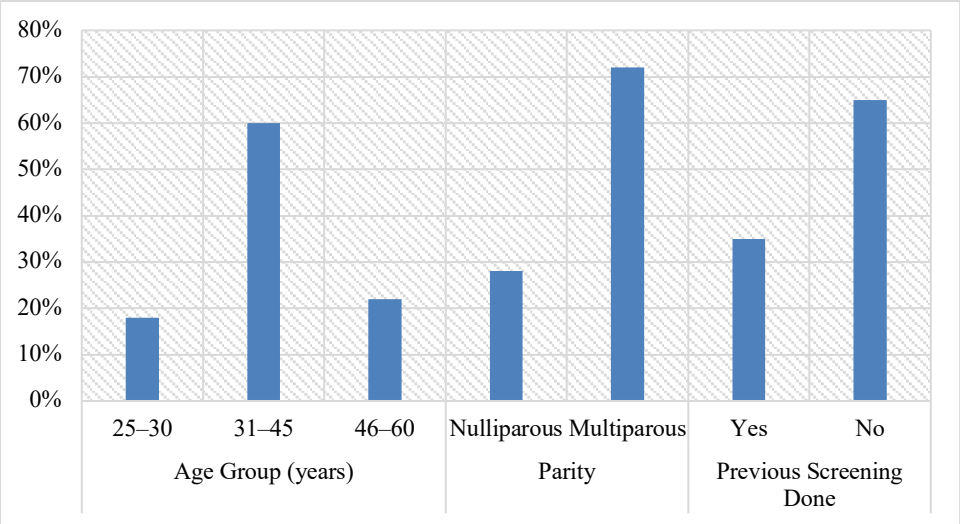


**Figure 1: Demographic Characteristics of the Study Population**

**Detection of Pre-Invasive Lesions:**

Of the 300 women screened, 64 (21.3%) had pre-invasive lesions confirmed by colposcopy and biopsy. The detection rates of each screening modality were as follows:

**Table 2: Detection Raes by Screening Method**

| Screening Method | Positive Cases Detected | Detection Rate (%) |
|---|---|---|
| Pap Smear | 40 | 13.3% |
| VIA | 48 | 16.0% |
| LBC | 52 | 17.3% |
| HPV DNA | 60 | 20.0% |
| Colposcopy (Gold Std) | 64 | 21.3% |

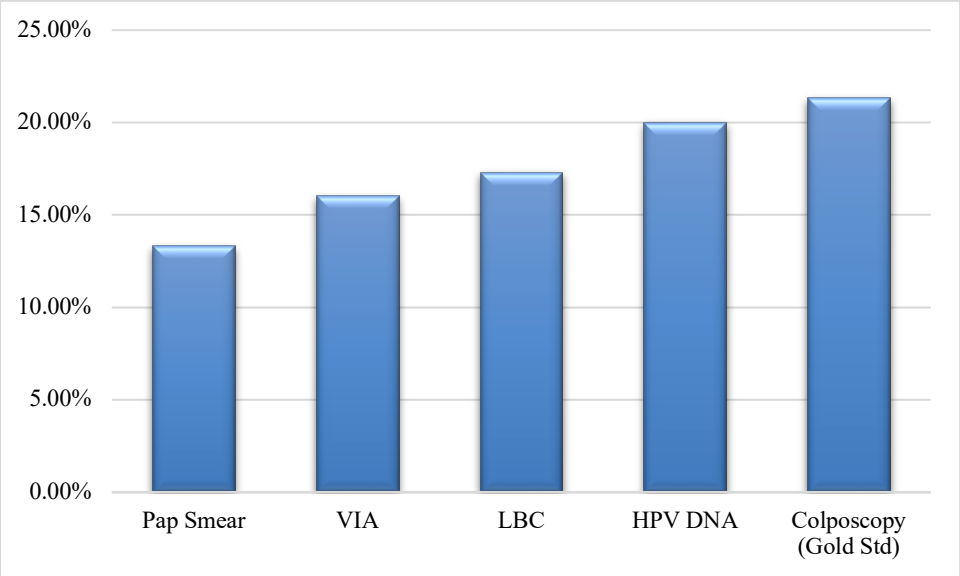


**Figure 2: Detection Rate by Screening Method**

The table emphasizes the number of positive cases identified and the detection rates of four cervical cancer screening tests—Pap Smear, VIA, LBC, and HPV DNA testing—against the gold standard of colposcopy. HPV DNA testing identified the most positive cases (60) and had a 20.0% detection rate, followed by LBC with 52 identified cases and a detection rate of 17.3%. VIA also demonstrated a fairly good detection rate of 16.0% and detected 48 positive cases. Pap smear, though commonly applied, recorded the lowest detection rate of 13.3% and detected only 40 cases. The gold standard, colposcopy, had the highest number of cases detected with a detection rate of 21.3% to confirm that the rest of the screening tools tend to underestimate the actual number of positive cases. Generally, HPV DNA testing was the most sensitive, followed by LBC, while VIA and Pap smear were least effective compared to the others.

### Diagnostic Accuracy

When compared with colposcopy and biopsy, the sensitivity, specificity, PPV, and NPV for each screening mode were determined.

**Table 3: Diagnostic Performance of Screening Modalities**

| Screening Method | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
|---|---|---|---|---|
| Pap Smear | 62.5 | 93.3 | 70.0 | 90.2 |
| VIA | 75.0 | 88.5 | 64.6 | 92.4 |
| LBC | 81.3 | 91.4 | 71.2 | 94.1 |
| HPV DNA | 93.8 | 85.5 | 66.7 | 97.7 |

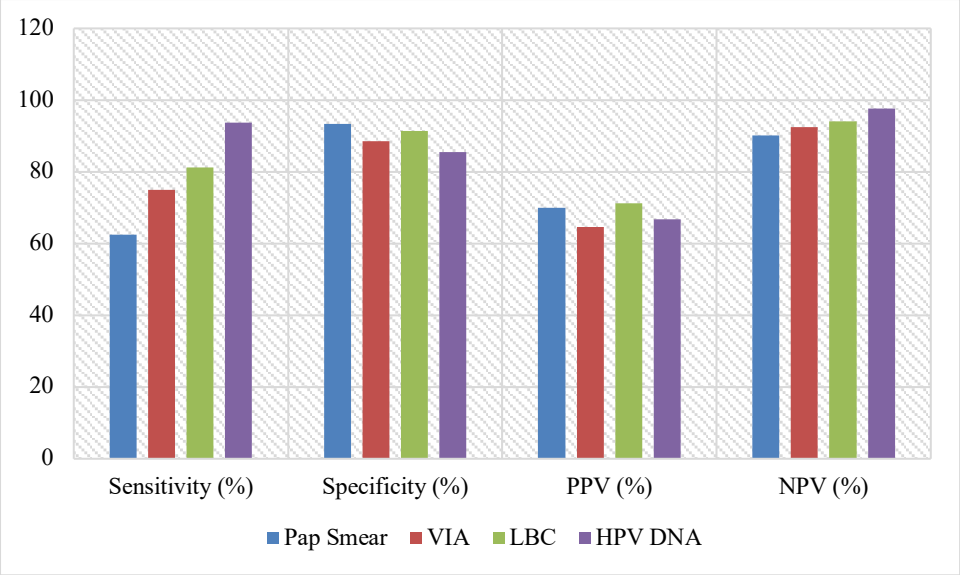


**Figure 3: Diagnostic Performance of Screening Modalities**

The figure indicates the diagnostic accuracy of four screening tests for cervical cancer: HPV DNA test, LBC, VIA, and Pap smear. HPV DNA test showed the highest sensitivity (93.8%) and NPV (97.7%), being most useful to identify pre-invasive lesions, and it provides the maximum confidence to exclude disease in the event of a negative test. LBC had a balanced performance, with sensitivity (81.3%) and NPV (94.1%) being better than Pap smear and VIA, which implies that it performs well in the detection of lesions as well as in giving reliable negative results. VIA had moderate sensitivity (75%) and specificity (88.5%), implying that it detects most cases but can also cause some false positives. Pap smear, while being most specific (93.3%), was least sensitive (62.5%), i.e., it failed to detect a large number of pre-invasive lesions. HPV DNA testing was found to be the most specific overall, especially for the true positives, while LBC offered a good alternative with a good combination of sensitivity and NPV.

## Discussion

This research proved that HPV DNA testing was most sensitive (93.8%) and most had NPV (97.7%) and therefore was the best in screening pre-invasive cervical cancer lesions. Pap smear, however, had the highest specificity (93.3%) but the lowest sensitivity (62.5%), which is that it could potentially miss a large number of early lesions.

## Comparison with Existing Literature

The results were consistent with a number of earlier studies that had shown greater sensitivity of HPV DNA testing compared to traditional cytology. Sankaranarayanan et al. and others also concluded in similar studies that molecular testing identified more high-grade lesions than cytological techniques alone. Although VIA is a low-cost and effective method in resource-poor settings, its lower specificity results in increased false positives, which can lead to unnecessary referrals.

LBC demonstrated enhanced performance compared with traditional Pap smear, in agreement with global data indicating increased sample adequacy and improved cellular representation.

## Clinical and Public Health Implications

With the high sensitivity and negative predictive value, HPV DNA testing may be regarded as the first-line screening test, particularly in organized screening programs. Still, because of cost and infrastructure constraints in most areas, VIA and LBC may remain useful, at least for mass screening in rural or underserved areas.

## Limitations of the Study

- The research was carried out within a single tertiary care hospital, and this may hinder generalizability.
- No follow-up measurements of progression or regression of lesions were included.
- Cost-effectiveness analysis was not conducted.

## Recommendations

- HPV DNA testing included in national guidelines for screening where appropriate.
- Ongoing use of VIA and LBC in low-resource settings with quality control.
- Additional research with cost-effectiveness and longitudinal follow-up assessments are warranted.

## Conclusion

This research showed that of the tested screening modalities for the detection of pre-invasive cervical cancer lesions, HPV DNA testing was the most

sensitive and had the highest negative predictive value and hence is the best tool for early detection. Liquid-Based Cytology (LBC) also had better diagnostic accuracy than the traditional Pap smear, and Visual Inspection with Acetic Acid (VIA) was a cost-effective, though moderately accurate, alternative that may be useful where resources are limited. While the Pap smear was still a specific test, its reduced sensitivity highlighted its shortcomings in isolated application. The report stressed the necessity of incorporating more sensitive screening tests such as HPV DNA testing into national cervical cancer screening programs to improve early detection and prevention. Nevertheless, given the differences in resource availability, a combination or tiered strategy using VIA and LBC might still be effective in various settings. This research validated the role of affordable, accurate, and prompt cervical cancer screening in decreasing disease burden and enhancing women's health outcomes.

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