

Research Article

Evaluation of the Performance of Self-sampling Versus Clinician-collected Sampling for Cervical Cancer Screening

Dropadi Kumari Meena¹, Aradhana Singh², Raj Kishore Singh³, Mudit Chauhan⁴

¹Junior Resident 3rd Year, ²Professor, Obstetrics & Gynaecology, BRD Medical College, Gorakhpur, Uttar Pradesh, India.

³Professor, General Medicine, BRD Medical College, Gorakhpur, Uttar Pradesh, India.

⁴Senior Resident, Department of Community Medicine, BRD Medical College, Gorakhpur, Uttar Pradesh, India.

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Corresponding Author:

Mudit Chauhan, Department of Community Medicine, BRD Medical College, Gorakhpur, Uttar Pradesh, India.

E-mail Id:

mudit4deal@gmail.com

Orcid Id:

<https://orcid.org/0000-0002-9418-3623>

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A B S T R A C T

Introduction: Regional variations exist in the incidence and mortality rates of cervical cancer, with higher rates observed in low- and middle-income countries (LMICs) compared to high-income countries. This difference can be attributed to the implementation of standardised screening systems in high-income countries. In LMICs, cervical cancer is the second most prevalent cancer and ranks as the third leading cause of cancer-related deaths among women. Importantly, women in LMICs face a higher lifetime risk of developing cervical cancer, estimated at 1.6%, compared to the 0.9% risk observed in high-income countries. The objective of the study was to compare the effectiveness of self-sampling and clinician-collected sampling methods for cervical cancer screening.

Methods: The sample included 100 participants and a total of 200 samples were collected (2 samples from each participant). This cross-sectional study spanned one year, from July 1, 2021, to June 30, 2022. Non-pregnant women aged 30-70 years were recruited as participants. The collected data underwent appropriate statistical analysis.

Results: The study results indicated that 88% of participants tested negative for HPV DNA according to the clinician's assessment, while 12% tested positive, and none had an inhibition result. In terms of the HPV DNA impression by clinicians, 12% of participants had a positive result, while 88% had a negative result.

Conclusion: The study revealed nearly equal HPV DNA positivity between self-sampling and clinician-collected samples, with significant agreement and high sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

Keywords: Self-sampling, Cervical Cancer, Pap Smear

Introduction

Cervical carcinoma is a leading cause of morbidity and mortality among gynaecologic cancers worldwide.¹ In Latin America, it is the second most prevalent cancer among women. Globally 604,000 new cases and 342,000 deaths were reported in the year 2022.² Human Papillomavirus (HPV) vaccination and cervical screening are effective strategies for prevention, but barriers such as acceptance and cost hinder implementation.³ Screening approaches include cytology, co-testing, primary HPV testing, and visual inspection with acetic acid (VIA).⁴ VIA has demonstrated efficacy in reducing cervical cancer mortality and is recommended in resource-limited settings.^{5,6} HPV testing has higher sensitivity and negative predictive value compared to cytology and is suitable for primary screening.^{7,8} Improvements in screening technologies, like liquid-based cytology (LBC), offer advantages in sample quality and automation.^{9,10} Self-sampling with HPV testing has shown promise in increasing coverage.^{11,12} HPV vaccination programmes in India have shown positive outcomes.^{13,14} International guidelines aim to enhance management and care for cervical cancer patients.^{16,17}

Epidemiology

Cervical cancer poses a significant global health challenge, with a reported 569,847 new cases and 311,365 deaths in 2018. The incidence and mortality rates of cervical cancer exhibit regional variations, with high-income countries benefiting from lower rates due to the implementation of standardised screening systems. On the other hand, in low- and middle-income countries (LMICs), cervical cancer ranks as the second most prevalent cancer and the third leading cause of cancer-related deaths among women. Notably, women in LMICs face a higher lifetime risk of developing cervical cancer (1.6%) compared to their counterparts in high-income countries (0.9%). In the United States, diagnoses typically occur around the age of 47 years, and advanced stages of the disease are more commonly observed in older women. Cervical cancer significantly contributes to cancer-related mortality in Africa and Latin America.¹⁸⁻²¹

Impact of HIV Infection

Sub-Saharan Africa carries the highest burden of HIV infections, accounting for over 70% of cases globally. Women with HIV are at an increased risk of HPV infection and have a higher likelihood of developing cervical cancer, often at a younger age. The rise in cervical cancer cases in South Africa may be linked to increased HIV infections due to expanded antiretroviral therapy use. Unlike other AIDS-related diseases, cervical cancer incidence remains unchanged despite antiretroviral therapy, as chronic immunosuppression is a risk factor for virus-associated

malignancies. Managing cervical cancer in HIV-positive women poses challenges due to tumour-virus interactions, T-cell dysfunction, treatment complications, and staging difficulties.²²⁻²⁴

Clinical Presentation and Diagnosis

Cervical cancer is often asymptomatic during its early stages, highlighting the importance of routine screening and pelvic examinations for detection. However, certain symptoms may arise as the disease progresses. These symptoms can include abnormal or post-coital bleeding, and in rare cases, a significant and foul-smelling vaginal discharge. When cancer invades the pelvic sidewall, it can manifest as lower limb oedema, flank pain, or sciatica. Bladder invasion may lead to the passage of urine through the vagina (vesicovaginal fistula), while the invasion of the rectum can result in the passage of faeces through the vagina (rectovaginal fistula).²⁵⁻²⁷ The diagnostic process involves several steps. It typically begins with a cervical biopsy to obtain a tissue sample for histopathological evaluation. Pelvic examinations are conducted to visualise the cervix and vaginal mucosa, and cervical cytology is performed. In symptomatic individuals or those with suggestive cytology results, colposcopy and biopsy are performed. In cases where cervical biopsy histology does not confirm the suspicion, a cone biopsy may be necessary for further evaluation.

Screening

Almost all cases of cervical cancer are caused by human papillomavirus (HPV) infection. High-risk HPV strains, such as types 16 and 18, are responsible for over 99% of precancerous lesions and cervical carcinomas. Other high-risk genotypes, including types 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68, also contribute to cervical cancer cases. HPV infections are associated with malignancies in various anogenital and oropharyngeal sites. Cervical cancer typically presents as squamous cell carcinoma or adenocarcinoma. HPV infections can be transient, but the progression to dysplasia and invasion is crucial in cervical carcinogenesis. Treatment approaches for cervical intraepithelial neoplasia (CIN) depend on the severity, ranging from monitoring for CIN1 to interventions like cryotherapy, LEEP, or CKC for CIN2 and CIN3.²⁸

Carcinogenesis

In recent years, there has been growing interest in the use of HPV (human papillomavirus) testing as a primary screening method for cervical cancer. Studies, such as the Addressing the Need for Advanced HPV Diagnostics trial, have shown that HPV testing alone is as effective, if not more effective, than cytology (Pap smear) for primary cervical cancer screening.²⁹ These findings have led to significant advancements in the field, including

the update of the FDA labelling of the Roche Cobas HPV test in 2014 to include its indication for primary cervical cancer screening.³⁰ This recognition highlights the increasing acceptance and utilisation of HPV testing as a reliable method for the early detection of cervical cancer. Although guidelines still recommend cytology alone or co-testing for screening,³¹ the use of HPV testing as the primary screening method is gaining traction.³² HPV testing offers advantages such as easier collection, especially with self-swab testing, which eliminates the need for a pelvic examination. Challenges with HPV testing include cost, laboratory processing requirements, and turnaround time for results.³³ However, there are simpler, faster, and more affordable HPV testing systems available.³³ Colposcopy, a visual examination of the cervix, is traditionally performed after abnormal cervical cancer screening.³⁴ Visual methods like VIA and VILI have emerged as cost-effective and accurate screening approaches, particularly in resource-limited settings.³⁵ Digital colposcopy provides high-quality digital images of the cervix, allowing for better visualisation, patient education, documentation, quality control, and telemedicine consultations.³⁶ Artificial intelligence algorithms are being developed to assist in interpreting digital colposcopic images.³⁷

Objective of the Study

To evaluate the performance of self-sampling versus clinician-collected sampling for cervical cancer screening

Material and Methods

The study was designed to determine the effectiveness of self-sampling versus clinician-collected sampling for cervical cancer screening in the Gynaecology OPD at BRD Medical College, Gorakhpur. A cross-sectional study design was utilised to perform the study. Based on the assumed prevalence of cervical cancer attributed to HPV in India, which was estimated to be 29%, the sample size calculation was performed using the formula $N = (4 * P * Q) / (L * L)$. Using the values $P = 29\%$, $Q = 100 - 29 = 71\%$, and $L = 10\%$ (precision level), the formula yielded a sample size (N) of 82.36. However, for the sake of convenience and to increase the robustness of the study, the researchers decided to take 100 participants and 200 samples in total (2 samples from each participant). This allowed for a more comprehensive analysis and increased statistical power. Specifically, 100 samples were allocated to each group: self-sampling and clinician-collected sampling. The study period extended over one year, starting from July 1, 2021, and ending on June 30, 2022. In this study, the inclusion criteria encompassed women aged 30–70 years who were seeking care in the outpatient department, possessed a cervix and willingly provided consent for participation. Additionally, eligible participants were those who had not undergone cervical cancer screening with a PAP smear in the last 3 years.

Conversely, the exclusion criteria comprised pregnant women, individuals who had undergone a hysterectomy involving cervical removal, those in critical health conditions or experiencing active bleeding, individuals with a prior diagnosis of pre-cancerous cervical lesions or cervical cancer, individuals currently undergoing treatment for such conditions, those with physical or mental challenges that hindered participation, and individuals who declined to provide consent for screening.

The collected data underwent comprehensive statistical analysis to derive meaningful insights. Descriptive statistics, including measures such as means, standard deviations, medians, interquartile ranges, frequencies, and percentages, were computed to provide a concise summary of the data. These statistical measures were employed to effectively summarise and present the key characteristics and trends observed in the dataset. Statistical tests including chi-square tests were employed to compare continuous and categorical variables between the two groups, as appropriate. ROC analysis was done to analyse sensitivity and specificity. The significance level was set at $p < 0.05$.

The study design received ethical clearance from the Institutional Ethics Committee, ensuring the protection of participants' rights and well-being. The intervention involved providing self-sampling kits and explaining the self-sampling procedure to eligible participants. Self-sampling participants were instructed to collect their cervical samples using a cervical cell sampler and a pre-labelled Digene HPV collection tube. For the clinician-collected sampling group, samples were obtained by clinicians using a brush after inserting a speculum. The collected samples underwent HPV DNA testing using recommended techniques such as microscopy of Papanicolaou-stained smears and RT-PCR.

Results

In this study of 100 non-pregnant women aged 30-70 years, the average age was 41.72 years. Most participants were below 60 years of age (92%), and the majority belonged to the Hindu religion (92%). The husbands had various occupations, with farmers being the largest group (60%), while most wives were housewives (96%). Addictions were reported by a small percentage, with 1% of wives reporting alcohol use and 1% reporting smoking, and among husbands, 11% reported alcohol use, 21% reported smoking, and 13% reported tobacco use. None of the participants had multiple sexual partners or received HPV immunisation or screening. The average parity was 3.22, and 68% of participants had high-risk behaviour. Education levels varied, with 43% being illiterate, 52% having primary school education, and 5% having intermediate education. Abnormal bleeding and dyspareunia were reported by a minority of participants. The average age at menarche was 13.40 years, and 26% of participants had attained

menopause. Socioeconomic status was mostly low (72%), and comorbidities were present in 35% of participants. Various findings were observed in the cervix, and only 10% of participants had undergone a pelvic examination (Table 1).

In the study, 89% of participants (self-assessment) tested negative for HPV DNA, while 10% tested positive and 1% had an inhibition result. Regarding the HPV DNA impression, 10% of participants had a positive result, while 89% had a negative result. On analysing HPV genotypes, it was found that 90% of participants had negative/ inhibition results, 6% tested positive for genotype 16, 2% for genotype 56 and 1% each tested positive for genotypes 51 and 58 (Table 2).

In the study, 88% of participants tested negative for HPV DNA according to the clinician's assessment, while 12% tested positive and none had an inhibition result. Regarding

the HPV DNA impression by clinicians, 12% of participants had a positive result, while 88% had a negative result. On analysing HPV genotypes as determined by clinicians, it was seen that 88% of participants had negative/ inhibition results, 7% tested positive for genotype 16, 1% for genotype 58 and 2% each tested positive for genotypes 51 and 56 (Tables 3 and 4).

The two methods demonstrated a strong agreement, with 98% of the results being consistent and only 2% showing discrepancies. This agreement was statistically significant, as indicated by Cohen's Kappa (0.898) with $p < 0.001$. When evaluating the diagnostic performance of HPV DNA Impression (self) in predicting HPV DNA Impression (clinician) as positive, the following metrics were observed: sensitivity: 83.3%, specificity: 100.0%, positive predictive value (PPV): 100.0%, negative predictive value (NPV): 97.8%, and diagnostic accuracy: 98.0% (Table 5).

Table 1. Distribution of Sociodemographic and Clinical Presentation

Clinical Details	Mean \pm SD Median (IQR) Min-Max OR n (%)
Age (years)	41.72 \pm 10.38 39.00 (33.00-49.00) 30.00 - 76.00
Age group (years)	
< 60	92 (92.0)
> 60	8 (8.0)
Religion	
Hindu	92 (92.0)
Muslim	8 (8.0)
Occupation of husband	
Business	24 (24.0)
Farmer	60 (60.0)
Others	16 (16.0)
Occupation of wife	
Business	1 (1.0)
Teacher	3 (3.0)
Housewife	96 (96.0)
Addictions of wife	
None	98 (98.0)
Alcohol	1 (1.0)
Smoking	1 (1.0)
Addictions of husband	
None	55 (55.0)
Alcohol	11 (11.0)

Smoking	21 (21.0)
Tobacco	13 (13.0)
Multiple sexual partners (yes)	0 (0.0)
Early onset of sexual activity (< 18 years) (yes)	58 (58.0)
Immunisation against HPV (yes)	0 (0.0)
Screening against HPV (yes)	0 (0.0)
Parity	3.22 ± 1.80 3.00 (2.00-4.00) 0.00 - 12.00
High-risk group/ high-risk behaviour (yes)	68 (68.0)
Education	
Illiterate	43 (43.0)
Primary school	52 (52.0)
Intermediate	5 (5.0)
Abnormal bleeding	
None	57 (57.0)
Post-menopausal	7 (7.0)
Irregular bleeding	15 (15.0)
Heavy menstrual bleeding	20 (20.0)
Post-coital bleeding	1 (1.0)
Dyspareunia (yes)	6 (6.0)
Age at menarche (years)	13.40 ± 1.39 13.00 (12.00-14.00) 11.00 - 18.00
Dysmenorrhoea (present)	16 (21.6)
Menopause (attained)	26 (26.0)
Socioeconomic status	
High	1 (1.0)
Middle	27 (27.0)
Low	72 (72.0)
BMI (kg/m²)	22.37 ± 2.87 22.40 (19.80-24.45) 14.30 - 28.40
Comorbidities (yes)	35 (35.0)
Cervix findings	
Healthy	19 (19.0)
Cervical erosion/ bleed on touch/ congestion	13 (13.0)
Cervical/ vaginal discharge	45 (45.0)
Cervical erosion with white discharge	19 (19.0)
Nabothian/ follicles/ polyp	4 (4.0)
Pelvic examination (Conducted)	10 (10.0)

Table 2. Summary of Parameters of Self-sampling

Parameters (Self)	Mean \pm SD Median (IQR) Min-Max OR n (%)
HPV DNA	
Negative	89 (89.0)
Positive	10 (10.0)
Inhibition	1 (1.0)
HPV DNA impression (positive)	10 (10)
HPV genotype	
Negative/ inhibition	90 (90)
Positive 16	6 (6)
Positive 51	1 (1.0)
Positive 56	2 (2.0)
Positive 58	1 (1.0)

Table 3. Summary of Parameters of Clinician Sampling

Parameters (Clinician)	n (%)
HPV DNA	
Negative	88 (88.0)
Positive	12 (12.0)
Inhibition	0 (0.0)
HPV DNA impression (Positive)	12 (12.0)
HPV genotype	
Negative/ inhibition	88 (88.0)
Positive 16	7 (7.0)
Positive 51	2 (2.0)
Positive 56	2 (2.0)
Positive 58	1 (1.0)

Table 4. Summary of HPV DNA Impression

HPV DNA Impression	Positive n (%)	Negative n (%)
Self*	10 (10.1)	89 (89.9)
Clinician	12 (12.0)	88 (88.0)

*1 (1%) was inhibition in self-sampling HPV DNA impression.

Table 5. Comparison of HPV DNA Impression (Self) with HPV DNA Impression (Clinician) (N = 99*)

HPV DNA Impression		HPV DNA Impression (Clinician)			Cohen's Kappa	
		Positive n (%)	Negative n (%)	Total N (%)	k	p Value
HPV DNA Impression (Self)	Positive	10 (10.1)	0 (0.0)	10 (10.1)	0.898	< 0.001
	Negative	2 (2.0)	87 (87.9)	89 (89.9)		
	Total N (%)	12 (12.1)	87 (87.9)	99 (100.0)		

*1 (1%) was inhibition in self-sampling HPV DNA impression.

Discussion

The clinical profile of the participants revealed that the mean age was 41.72 ± 10.38 years. The majority of participants were Hindu (92%), while a smaller proportion were Muslim (8%). Regarding education, 43% of participants were illiterate, while 52% had primary and the rest were intermediate. The mean parity was 3.22 ± 1.80 , and most participants (58.0%) reported an early onset of sexual activity (before 18 years). Notably, none of the participants reported having multiple sexual partners. Abnormal bleeding was observed in 43% of participants, including post-menopausal bleeding, irregular bleeding during menstruation, heavy menstrual bleeding, and post-coital bleeding. Dyspareunia was reported by only 6.0% of participants. These findings are consistent with similar studies conducted by Hwang et al.³⁸ and Shanmugapriya and Devika,³⁹ which reported comparable demographic and clinical characteristics.

The outcome of HPV testing by self-screening showed that 89.9% of participants tested negative for HPV DNA, while 10.1% tested positive. Among the positive cases, HPV genotypes 16, 51, 56 and 58 were detected. This aligns with findings from studies conducted by Hwang et al.,³⁸ Chen et al.,⁴⁰ Ketelaars et al.,⁴¹ and Lindström et al.,⁴² which reported varying HPV positivity rates and genotypes. In contrast, Bhatla et al. found a higher HPV positivity rate (18.75%) among women in their study.⁴³

When HPV testing was performed by a clinician, 88.0% of participants tested negative for HPV DNA, while 12.0% tested positive. Similar to self-screening, HPV genotypes 16, 51, 56 and 58 were detected. These findings are consistent with the study conducted by Bhatla et al.⁴³ but differ from studies by Ertik et al.⁴⁴ and Leinonen et al.⁴⁵, which reported higher rates of HPV positivity.

Conclusion

The study found that almost equal numbers of participants tested positive for HPV DNA using self-sampling and clinician-collected sampling. Statistical analysis showed significant agreement between the two methods (Cohen's Kappa = 0.898, $p < 0.001$), with high sensitivity (83.3%),

specificity (100%), PPV (100%), and NPV (97.8%). Similar results were observed for specific HPV genotypes. The majority of participants were willing to perform self-testing due to comparable results. Overall, self-sampling showed promise as an effective alternative for cervical cancer screening.

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