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Original Research Article

Cervical cancer screening in patients at a tertiary care centre with Pap smear and HPV DNA testing

Khushboo Suresh Shinde[1]*, Swati Kochar[1], Asmita Nayak[1], Anjli Gupta[2], Chandni Soni[1], Bhawana Charan[1]

[1]Department of Obstetrics and Gynecology, Sardar Patel Medical College, Bikaner, Rajasthan, India
[2]Department of Microbiology & Immunology, Sardar Patel Medical College, Bikaner, Rajasthan, India

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***Correspondence:**
Dr. Khushboo Suresh Shinde,
E-mail: 96kshinde@gmail.com

ABSTRACT

Background: Cervical cancer ranks fourth among the most commonly diagnosed cancers as well as the fourth leading cause of cancer mortality in women globally. Of all new cases and deaths worldwide in 2020, India accounted nearly one-fourth of deaths due to cervical cancer. In India, cervical cancer is the second most common cancer in both incidence 18.3% and cancer mortality 18.7% among women in 2020, with a 5-year prevalence of 18.8%.
Methods: A hospital based cross sectional study was conducted in the Gynecology OPD of PBM Hospital, Bikaner. 118 women aged 19-60 years presenting with complaints such as unusual bleeding between periods/after menopause/after sexual intercourse; increased or foul-smelling vaginal discharge etc were included. A questionnaire was administered containing general information, clinical findings at pelvic evaluation. They then underwent Pap smear, HPV testing and histo-pathology. Appropriate statistical tests were used to compare the outcome between the sub-groups.
Results: Pap smear offered high specificity (~93.9%) and a strong NPV (99.1%), with a low positive predictive value (PPV~18%-25%) indicating a high false-positive rate, necessitating triage with confirmatory tests. HPV DNA testing emerged as the superior tool, with 100% sensitivity and NPV. Its specificity was over 95% and PPV was 37.5%.
Conclusions: HPV DNA testing is the most accurate screening test, reflecting its utility in early detection of high-risk cases.

Keywords: Transformation zone, High risk, Human papilloma virus, Loop electrosurgical excision procedure, Cold knife conization

INTRODUCTION

The cervix is the lower, narrow portion of the uterus that connects the uterus to the vagina. It is approximately 2–4 cm in length and is divided into two main parts, the ectocervix and the endocervix. The transformation zone (TZ) is the area where the squamous epithelium of the ectocervix meets the columnar epithelium of the endocervix. This is the most common site for cervical cancer (squamous cell carcinoma) and HPV infection. Cervical cancer ranks fourth among the most commonly diagnosed cancers as well as the fourth leading cause of cancer mortality in women globally.[1] Of all new cases and deaths worldwide in 2020, India accounted for approximately one-fifth of new cases and nearly one-fourth of deaths due to cervical cancer. In India, cervical cancer is the second most common cancer in both incidence (18.3%) and cancer mortality (18.7%) among women in 2020, with a 5-year prevalence of 18.8%.[2] The major risk factor for cervical cancer is persistent infection with high risk (HR) human papilloma virus (HPV). The most common HPV types in patients, in descending order of frequency, were types 16, 18, 45, 31, 33, 52, 58 and 35. About 5% of women in the general population in India are estimated to harbour cervical HPV-16/18 infection at a given time, and 83.2% of invasive cervical cancers are attributed to HPVs 16 or 18.[3] Through micro-wounds, HPV infects the basal cells of the stratified cervical

epithelium. The virus internalizes by endocytic uptake and, sequentially, in endosomal compartments, the viral capsid binds to retromer components such as Sortin-nexin 17 and 27, helping the L2-DNA complex to escape lysosomal degradation to be then transported to the nucleus via dynein-mediated transport through microtubules.[6] Synthesized E1 and E2 interact with the origin of replication site in the LCR. As the epithelium differentiates, the expression of the early viral genes, including E5 and E4, augments in the middle and upper layers, and genome amplification increases.[7] E5 maintains cell proliferation and delays cell differentiation by modulating EGF/KGF receptor activities, complementing the functions of E6 and E7.[8] L1 and L2 capsid proteins are produced in the differentiated keratinocytes, where virions are assembled and released due to the disruption of the cytoskeleton promoted by the E4.[9]

Among HPV attributable cancers, 80% are cervical cancer which are preventable through HPV vaccination along with other HPV related cancers. In 2018, World Health Organization has called for a global action towards elimination of cervical cancer (a threshold of 4 per 100,000 women-year) and set 90-70-90 targets to be achieved by 2030.[10] Many of the women are asymptomatic and are diagnosed at late stages. Symptoms of cervical cancer are abnormal vaginal bleeding, bleeding between periods (intermenstrual bleeding), heavier or longer menstrual periods, postmenopausal bleeding or postcoital bleeding (bleeding after sexual intercourse). Women can have unusual watery, bloody, or foul-smelling vaginal discharge.

As the cancer spreads, symptoms become more severe. They can have persistent dull or sharp pain in the lower abdomen or pelvis, dysuria or haematuria. Systemic symptoms appear due to cancer spread or chronic inflammation. Screening programme has proved effective in reducing incidence of invasive cancer by 80% and mortality by 60%. Cervical cancer screening is crucial for early detection and prevention.

METHODS

A hospital based prospective study was conducted in the Gynecology OPD of PBM Hospital, Bikaner from June 2024 to May 2025. A sample size of 118 females was taken at 95% confidence level and 5% absolute error. We included non-pregnant women aged 19-60 years, willing to participate, presenting with complaints such as unusual bleeding between periods/after menopause/after sexual intercourse; increased or foul-smelling vaginal discharge; persistent pain in the back/legs/pelvis; weight loss etc. The main objective was to study the efficacy of PAP Smear and HPV testing by comparing the sensitivity, specificity, positive predictive value and negative predictive value. Based on the eligibility criteria, the participants were screened and selected from the OPD after a written and informed consent. Selected participants were interviewed using a semi-structured questionnaire with general information on each woman, clinical findings at pelvic evaluation, results of the Pap smear, HPV testing. Patients were placed in lithotomy position. A Pap smear sample was then taken using a conventional wooden Ayres spatula and endocervical brush. The smear was then fixed with 95% ethanol for 30 minutes and sent to pathology department. The results of the Pap smear were reported according to the 2014 Bethesda system for reporting cervical cytology.

HPV DNA testing was done using a vaginal and a cervical sample. Sample was collected using disposable swab and then inserted in the liquid media provided and stored at -20°C till processing. We used Hi-PCR® Human papilloma virus genotyping (16,18,45) multiplex probe PCR Kit for HPV DNA detection. It is a standard, non-invasive, simple and fast method for diagnosis. Real time PCR/ quantitative PCR (qPCR) is a lab technique based on the principle of PCR. It detects HPV 16 in FAM channel, HPV 18 in Texas Red channel and HPV 45 in JOE channel and an internal control in cy5 channel.

It allows detection of these in a single tube multiplex reaction. All PAP smear positive cases and HPV DNA positive were followed by cervical biopsy for confirmation. The data was entered and analysed systematically. Appropriate statistical tests were used to compare the outcome between two sub-groups, considering cervical biopsy as the gold std. Quality assurance was ensured.

RESULTS

A total of 118 women were evaluated, ranging in age from 19 to 60 years after considering the inclusion and exclusion criteria. Socio-economic and baseline characteristics of study participants are as displayed in Table 1. The mean age of the patients was 37.09 years, with a standard deviation (SD) of 10.63 years, indicating a moderately broad spread of ages within the population. The overwhelming majority of patients in the sample were multiparous, accounting for 87.1% (104 out of 118 cases). Regular cycles were reported in 66.1% of the patients (78 out of 118 cases). Irregular cycles occurred in 33.9% of the patients. Upper lower class was the largest group, comprising 67 cases, accounts for 56.78% of the total. This indicates a significant burden of cervical cancer among individuals with lower income and limited education or semi-skilled occupations.

Multiple symptoms were reported by the same individual. White discharge was the most common symptom, affecting ~86% of patients. 94 patients had Pain in lower abdomen as one of the complaints. Backache was also present in majority (84 cases). Itching around vulva was present in 47 cases and another 47 had dysuria (painful urination). Irregular periods were reported by 41 cases. This was followed by dyspareunia, menorrhagia, contact bleeding, postmenopausal bleeding. On per-speculum examination, it was found that 66.94% of women had an

inflamed cervix, and 56.77% showed signs of vaginitis. Hypertrophied cervix was present in 38.13%, while 49.15% had a normal cervix. Bleeding on touch, ulcerative or irregular growths, ectopy and polyps were also found. PAP smear cytology analysis showed that 92.37% had NILM.

The remaining 7.63% showed abnormalities, including ASCUS in 2 cases (1.69%), ASC-H in 2 cases (1.69%), LSIL in 3 cases (2.54%), HSIL: 1 case (0.85%) and Squamous cell carcinoma in 1 case (0.85%). Out of 118 patients, 8 tested positive (6.8%) for high-risk HPV. The genotype being 5 cases positive for HPV 16, 1 for HPV 45, 1 case had HPV 16 and 18 co-infection and 1 case had HPV 18 and 45 co-infections. Biopsies were conducted for women reporting any of the 3 screening tests as positive or a strong suspicion on examination.

Out of 118 cases, 115 cases (97.46%) were negative for malignancy. 2 cases (1.69%) showed dysplasia while 1 case (0.84%) was confirmed as squamous cell carcinoma. Table 2 shows the sensitivity of pap smear in comparison with HPV DNA status to be 62.5%. Specificity was 96.36%, positive predictive value (PPV) was found to be 55.6% while the negative predictive value (NPV) was 97.2% meaning if the PAP smear was negative, it was very likely correct. The p value was found to be <0.001 indicating a statistically significant correlation between PAP smear results and HPV DNA test results.

Table 3 compares pap smear cytology results with biopsy findings. Sensitivity of PAP test was 66.67%. Specificity was 93.91%. PPV was 22.2% indicating that a positive pap smear result alone has limited predictive value, requiring confirmation by biopsy or colposcopy. NPV was 99.1%. Table 4 shows p value to be <0.001 indicating high statistical significance, meaning the correlation between HPV DNA test results and biopsy findings is not due to chance.

Sensitivity was 100% i.e. all individuals with a positive biopsy result (true cases) i.e. they were correctly identified by the HPV DNA test (no false negatives). Specificity was found to be 95.65%. PPV was found to be 37.5%, while the NPV was 100%, showing that when the test is negative, there is a 100% certainty the person does not have disease (no false negatives).

Table 1: Baseline characteristics of study participants (n=118).

Variables	Total	%
Age (in years)		
19-29	31	26
30-39	41	38
40-49	33	25
50 years and above	13	11
Parity		
Nullipara	2	1.69
1	12	10.98
2	37	31.35
3	28	23.72
4	23	19.49
≥5	16	13.56
Menstrual pattern		
Regular	78	66.1
Irregular	40	33.9
Socio-economic status		
Upper	2	1.69
Upper middle	11	9.32
Lower middle	24	20.34
Upper lower	67	56.78
Lower	14	11.86

Table 2: Comparison of Pap smear with HPV DNA status.

	HPV DNA positive (8)	HPV DNA negative (110)	P value	Sensitivity; Specificity	PPV; NPV
PAP smear positive (9)	5	4	<0.001	62.5%; 96.36%	55.6%; 97.2%
PAP smear negative (109)	3	106			

Table 3- Comparison of Pap smear results with histopathology.

	Biopsy positive (3)	Biopsy negative (115)	P value	Sensitivity; Specificity	PPV; NPV
PAP smear positive (9)	2	7	<0.001	66.67%; 93.91%	22.2%; 99.1%
PAP smear negative (109)	1	108			

Table 4: Association of outcomes on HPV DNA status with histopathology.

	Biopsy positive (3)	Biopsy negative (115)	P value	Sensitivity; Specificity	PPV; NPV
HPV DNA positive (8)	3	5	<0.001	100%; 95.65%	37.5%; 100%
HPV DNA negative (0)	0	110			

DISCUSSION

The present prospective study was conducted among 118 women presenting with high risk factors for development of cervical cancer at the Out Patient Department of Obstetrics and Gynecology in PBM Hospital, Bikaner. From our study we concluded that HPV DNA testing, though more expensive, offers superior accuracy, especially in populations at high risk. These results are similar to a study conducted by Sankaranarayanan et al in Southern India, where they compared the screening methods and found Pap smear sensitivity to be ~55–65%, specificity to be ~95–98%, the NPV was >96%. Joshi et al found that Pap smear sensitivity was 60.8% for detecting HPV-positive lesions, but specificity exceeded 93%. Kanthimathy et al conducted a study in Kerala, in which Pap smear showed sensitivity of 61%, specificity of 94%, and NPV of 98.2% when compared to HPV DNA.[11-13]

Our results are supported by previous literature. Gupta et al in his study found out the sensitivity of PAP smear cytology against biopsy to be 68%, specificity to be 92.4%, PPV to be 42% and NPV to be 96.3%. Buchade & Kanaka in yet another similar study found PAP's sensitivity to be 65%, specificity to be 94.8%, PPV to be 48.2% and NPV to be 96.7%. Also in one more study, Chaudhary et al found similar metrics on comparison of PAP and biopsy: Sensitivity: 70.2%, Specificity: 90.1%, PPV: 38%, NPV: 97%. Thus, Pap smear is a valuable, cost-effective screening test with excellent specificity but limited sensitivity (66.67%), making it vulnerable to false negatives.[14-16]

On comparing the diagnostic accuracy of HPV DNA testing against histopathological biopsy, the gold standard for identifying cervical intraepithelial neoplasia and carcinoma, it was found that the sensitivity of HPV DNA was 100% with a specificity of 95.65%, PPV of 37.50% and a NPV of 100%. Sankaranarayanan et al in his study found HPV testing sensitivity to be 100%, specificity to be ~92%, PPV to be 55–60% and NPV to be >99%.[11] Joshi et al in his study found HPV 16/18 DNA testing detected 100% of biopsy-confirmed high-grade lesions and had a specificity of 90.2%. Kanthimathy et al had similar results in his study with a sensitivity of 100%, Specificity of 93%, NPV of 100%.[12,13]

These findings validate HPV DNA testing as the most sensitive and reliable tool for early detection of cervical neoplasia. While false positives can occur due to transient or non-progressive HPV infections, the complete absence of false negatives makes it an ideal screening method. The high NPV (100%) ensures that a negative test result provides strong reassurance against cervical disease.

CONCLUSION

Cervical cancer remains one of the most preventable yet prevalent cancers among women worldwide. Despite being highly preventable through early detection and treatment, uptake of cervical cancer screening in India remains low, especially among women in rural and socioeconomically disadvantaged communities. This study provides a comprehensive evaluation of cervical cancer screening modalities among 118 women, using Pap smear and HPV DNA testing, with histopathology as the gold standard. The results reinforce that there is a need for early and effective cervical screening in the India, particularly among women from socioeconomically disadvantaged backgrounds.

HPV DNA testing emerged as the most accurate tool, reflecting its utility in early detection of high-risk cases. However, the cost and infrastructure requirements may limit its widespread use in primary care.

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