Indian Journal of Health Care, Medical & Pharmacy Practice (Vol 7, Issue 1, Jan-June 2026)
Home page of the journal: https://ijhmp.com/Home

Research Article

CORELATION OF HISTOPATHOLOGY, PAP SMEAR AND HPV GENOME IN SUSPICIOUS CERVICAL LESIONS

Dr. Vijay Kumar Bodal[1], Dr. Navpreet Kaur[2]*, Dr. Rahul Mahajan[3]

[1]Professor, Department of Pathology, Government Medical College, Patiala, Punjab, India.
[2]Assistant Professor, Department of Pathology, Dr BR Ambedkar State Institute of Medical Sciences, Mohali, Punjab, India.
[3]Senior Consultant, Department of Neurosciences, Max Hospital, Mohali, Punjab, India.

Corresponding Author*: Dr. Navpreet Kaur, Assistant Professor, Department of Pathology, Dr BR Ambedkar State Institute of Medical Sciences, Mohali, Punjab, India.

Email ID: dr.navpreet3489@gmail.com

Orcid Id: https://orcid.org/0000-0002-7891-107X

DOI: https://doi.org/10.59551/IJHMP/25832069/2026.7.1.139

How to cite this article: Bodal VK, Kaur N, Mahajan R. Corelation of Histopathology, Pap Smear and HPV Genome in Suspicious Cervical Lesions. *Indian J. Health Care, Med. Pharm. Pract.* 2026;7(1):312-318.

Received: 11 May, 2026, Decision for Acceptance: 15 June, 2026

ABSTRACT

Background: Cervical cancer remains one of the most common malignancies affecting women in developing countries, including India. Persistent infection with high-risk human papillomavirus (HPV) is now recognized as the most important etiological factor in cervical carcinogenesis. The present study was conducted to evaluate cervical cytology, histopathology, and HPV DNA status in women presenting with suspicious cervical lesions.

Methods: This observational cross-sectional study was conducted in the Department of Pathology, Government Medical College, Patiala, from January 2015 to June 2016. A total of 150 women with suspicious cervical lesions were included. Cervical smears, cervical brushings, cervical biopsies, and hysterectomy specimens were evaluated. Pap smears were reported according to The Bethesda System 2014, while histopathological lesions were classified according to WHO recommendations. HPV DNA testing was performed using the BD Onclarity HPV assay based on real-time polymerase chain reaction.

Results: Most patients belonged to the 31- 45 years age group (52.7%). Vaginal discharge was the most common presenting complaint (36%), followed by irregular bleeding (26%). Histopathological examination showed infection in 58.7%, dysplasia in 12.7%, benign lesions in 3.3%, and malignancy in 25.3% of cases. Squamous cell carcinoma was the most common malignant lesion (92.1%). HPV positivity was observed in 97.36% of malignant lesions and 57.89% of dysplastic lesions. HPV 16 was the most common genotype identified in malignant lesions (67.56%). Significant association was observed between increasing age, higher parity, HPV positivity, and cervical malignancy.

Conclusions: Infection with high-risk HPV, especially HPV 16, showed a strong association with cervical dysplasia and malignancy. Combined use of cervical cytology, histopathology, and HPV testing improves detection of premalignant and malignant cervical lesions.

KEYWORDS: Cervical Cancer, HPV DNA, Pap Smear, Histopathology, Cervical Cytology, HPV 16.

Introduction

Cancer of the cervix continues to be a major public health problem worldwide and remains one of the leading causes of cancer-related morbidity and mortality among women in developing countries. Despite advances in screening and preventive strategies, cervical carcinoma continues to pose a significant burden in low- and middle-income countries because of lack of awareness, poor screening coverage, limited healthcare accessibility, and delayed diagnosis. India contributes substantially to the global burden of cervical cancer, accounting for a considerable proportion of newly diagnosed cases and cancer-related deaths among women[1,2].

The cervix is particularly susceptible to neoplastic transformation because of the presence of the transformation zone, where squamous metaplasia is continuously active. Persistent exposure to endogenous and exogenous factors such as hormonal influences, early sexual activity, multiparity, poor genital hygiene, sexually transmitted infections, and smoking predisposes the cervical epithelium to dysplastic and neoplastic changes[3]. Persistent infection with high-risk human papillomavirus (HPV) is now considered an essential event in cervical carcinogenesis[4].

Human papillomavirus is a small non-enveloped DNA virus belonging to the Papillomaviridae family. More than 200 HPV genotypes have been identified, of which approximately 40 infect the anogenital tract[5,6]. Based on oncogenic potential, HPV types are broadly classified into high-risk and low-risk groups. High-risk HPV types, especially HPV 16 and HPV 18, are strongly associated with cervical intraepithelial neoplasia and invasive carcinoma[5,6]. Persistent infection with oncogenic HPV may lead to integration of viral DNA into the host genome, resulting in overexpression of viral oncogenes E6 and E7, which interfere with tumor suppressor proteins p53 and retinoblastoma protein, thereby promoting malignant transformation[7].

The relationship between HPV infection and cervical cancer has been extensively studied worldwide. Muyden et al[8]. demonstrated HPV positivity in 100% of cervical carcinoma cases using PCR-based techniques, while Jung et al[9]. reported HPV positivity in 96.3% of carcinomas and identified HPV 16 as the predominant genotype. Similarly, Bayo et al[10]. observed HPV prevalence of 96.9% among cervical cancer cases. Several studies have also emphasized the role of persistent HPV infection in progression from low-grade lesions to high-grade dysplasia and invasive carcinoma[11,12].

Cervical cytology using the Papanicolaou (Pap) smear has been one of the most successful cancer screening methods and has significantly reduced the incidence and mortality of cervical cancer in developed countries[13-15]. The Bethesda System has standardized reporting of cervical cytology and improved communication between pathologists and clinicians[16]. However, conventional cytology has limitations including false-negative results, obscuring inflammation, and sampling errors[17]. Histopathological examination remains the gold standard for diagnosis of premalignant and malignant cervical lesions.

In recent years, HPV DNA testing has emerged as a highly sensitive and objective method for detecting high-risk HPV infection. PCR-based methods are currently considered among the most sensitive techniques for HPV detection and genotyping[18]. Several studies have demonstrated that HPV DNA testing improves sensitivity for detection of high-grade lesions when combined with conventional cytology[19].

The present study was therefore undertaken to evaluate cervical cytological and histopathological changes in suspicious cervical lesions, to correlate these findings with HPV DNA detection, and to assess the role of HPV in cervical carcinogenesis.

Methods

Study Design and Setting

This observational cross-sectional study was conducted in the Department of Pathology, Government Medical College, Patiala, in collaboration with Rajindra Hospital, Patiala, from January 2015 to June 2016. The study was conducted as part of MD Pathology dissertation work after obtaining approval from the Institutional Ethics Committee. Written Informed consent was obtained from all study participants prior to enrolment.

Study Population

A total of 150 women presenting with gynecological complaints or suspicious cervical lesions in the Gynecology Outpatient Department were included in the study.

Inclusion Criteria

Women presenting with suspicious cervical lesions, abnormal cervical appearance, unhealthy cervix, vaginal discharge, postcoital bleeding, irregular bleeding, postmenopausal bleeding, or other gynecological complaints were included in the study.

Exclusion Criteria

Patients previously treated for carcinoma, patients unwilling to participate.

Clinical Evaluation

Detailed clinical history including age, parity, menstrual history and presenting complaints was recorded in all cases. Findings of local examination were also documented.

Cytological Examination

Cervical smears were collected and immediately fixed. Smears were stained using the Papanicolaou staining

ISSN 2583-2069

technique and reported according to The Bethesda System 2014. Smears were categorized as NILM, ASCUS/ASC-H, LSIL, HSIL, or malignancy.

Histopathological Examination

Cervical biopsies and hysterectomy specimens were fixed in 10% formalin, processed routinely, and stained with hematoxylin and eosin. Histopathological lesions were classified according to WHO recommendations.

HPV DNA detection

HPV DNA testing was performed using the BD Onclarity HPV Assay on the BD Viper LT System. The assay detects high-risk HPV genotypes including HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68. Cervical brushings were collected and processed according to manufacturer guidelines.

Statistical Analysis

Data obtained were entered into Microsoft Excel worksheet and analyzed statistically. Associations between variables were assessed using appropriate statistical methods. A p value of <0.05 was considered statistically significant.

Results

A total of 150 women with suspicious cervical lesions were evaluated in the present study. Most patients belonged to the reproductive age group of 31- 45 years (79), followed by 46- 60 years (53). The mean age of the study population was 45.72 years.

Vaginal discharge was the most common presenting complaint observed in 36% (54) of patients, followed by irregular bleeding in 26% (39). Postcoital bleeding and postmenopausal bleeding were more commonly associated with malignant lesions.

Majority of the women included in the study were multiparous. Higher parity demonstrated significant association with cervical malignancy. Most malignant cases were observed in women with parity greater than three.

On cervical cytology, NILM was the most common finding, accounting for 64.6% (97) cases. ASCUS/ASC-H was observed in 8.6% (13) cases, LSIL in 6%, (9) HSIL in 7.3%, (11) and frank malignancy in 12% (18) cases.

Histopathological examination revealed infection in 58.7% (88) cases, dysplasia in 12.7%(19), benign lesions in 3.3%(5), and malignancy in 25.3% (38) cases. Squamous cell carcinoma was the predominant histological type among malignant lesions, accounting for 92.1% (35) of malignant cases. Adenocarcinoma and small cell carcinoma constituted a small proportion of cases (Table 1, Figure 1).

Table 1:Correlation of Cytology and Histopathology Diagnosis

Histopathological Diagnosis	No.	Cytological Diagnosis					
		Inadequate	NILM	ASCUS/H	LSIL	HSIL	Ca
Infections	88	-	83	4	1	-	-
Benign tumors	5	-	4	-	-	1	-
Dysplasia	19	-	7	3	6	3	-
Carcinoma	38	2	3	6	2	7	18
Total	150	02	97	13	09	11	18

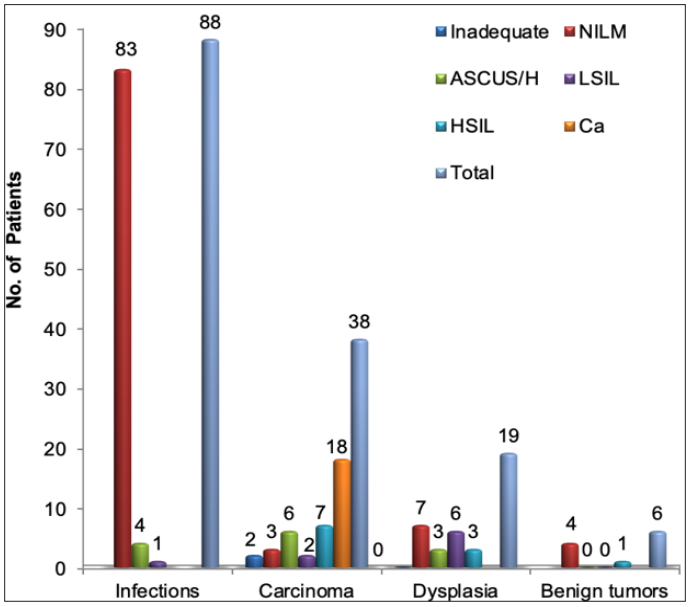

Figure 1.Correlation of Histopathology and Cytology Diagnosis

HPV positivity was observed in 56 out of 150 cases. Among malignant lesions, HPV positivity was detected in 97.36% cases, while dysplastic lesions demonstrated HPV positivity in 57.89% (11) cases. HPV prevalence in inflammatory lesions was significantly lower, p value <0.001 (Table 2,3,4) (Figure 2).

Table 2: HPV In Patients With Suspicious Cervix

Diagnosis	HPV present	HPV absent	Total	Percentage
Infection	8	80	88	9.09
Benign disease	-	5	5	00
Dysplasia	11	8	19	57.89
Malignancy	37	1	38	97.36
Total	56	94	150	

Table 3: Correlation Of HPV Infection With Malignancy

Malignancy	HPV present	HPV absent	Total	HPV prevalence
Present	37	1	38	97.36%
Absent	19	93	112	16.9%

Table 4: HPV Distribution In Malignant Cases

HPV	Squamous cell carcinoma	Adenocarcinoma	Small cell carcinoma
16	24	1	-
18	4	1	-
Others	7	-	-
Total	35	2	-

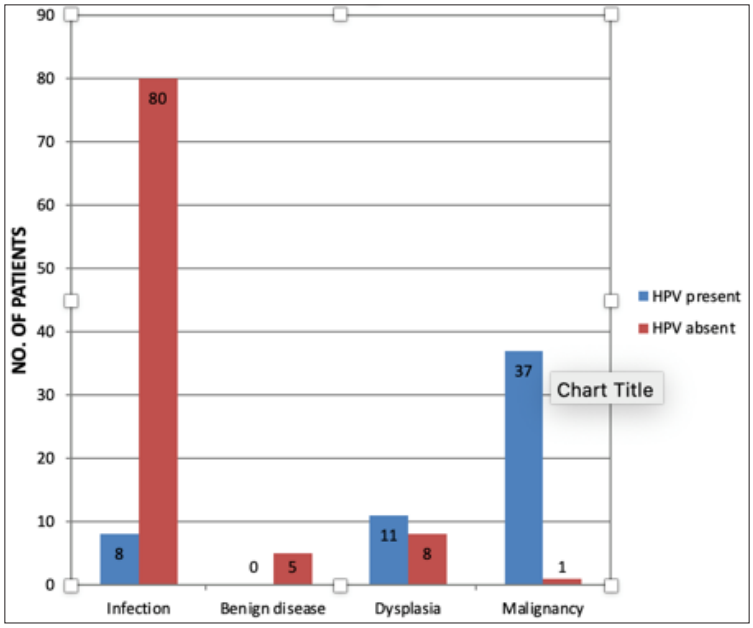

Figure 2.HPV in suspicious cervical lesions

HPV 16 was the most common genotype identified in malignant lesions, followed by HPV 18. Other high-risk HPV genotypes were detected in a smaller proportion of cases.

A statistically significant association was observed between increasing age and cervical malignancy (p value <0.001). Malignant lesions were more frequently seen in women above 46 years of age. Similarly, increasing parity showed significant correlation with malignancy (p value <0.001).

The present study demonstrated a markedly higher sensitivity of HPV testing compared with conventional Pap smear cytology for the detection of cervical malignancy. Using histopathology as the reference standard, HPV testing achieved a sensitivity of 97.37%, whereas Pap smear demonstrated a sensitivity of only 47.37%. This finding suggests that HPV testing is substantially more effective in identifying women with underlying cervical pathology and is less likely to miss clinically significant lesions.

ISSN 2583-2069

The specificity of Pap smear was 100%, indicating that all cytologically positive cases were confirmed on histopathology. Although this reflects the high reliability of a positive Pap smear result, the relatively low sensitivity highlights its limitation as a standalone screening tool. A considerable proportion of histopathologically confirmed lesions were not detected by cytology, emphasizing the possibility of false-negative results due to sampling errors, inadequate cellular representation, or interpretative limitations.

HPV testing demonstrated a specificity of 83.04%, which was lower than that of Pap smear because of the presence of false-positive results. However, its excellent negative predictive value of 98.94% indicates that women with a negative HPV test are highly unlikely to harbor significant cervical disease. This characteristic makes HPV testing particularly valuable for population-based screening programs and supports the longer screening intervals recommended in HPV-based screening strategies (Table 5,6).

Table 5: Correlation of HPV infection with malignancy

	Histopathology positive for malignancy	**Histopathology negative for malignancy**
HPV positive	37	19
HPV negative	1	93

Table 6: Correlation of Histopathology with Cytology

	Histopathology positive for malignancy	**Histopathology negative for malignancy**
Pap smear positive for malignancy	18	0
Pap smear negative malignancy	20	112

Discussion

Cervical cancer remains one of the most important malignancies affecting women in India despite the availability of screening methods and preventive strategies. The present study evaluated cervical cytology, histopathology, and HPV DNA status in women presenting with suspicious cervical lesions and correlated these findings with clinicopathological variables.

In the present study, the majority of patients belonged to the 31- 45 years age group, while malignant lesions were more common in women above 46 years of age. The mean age of patients with cervical carcinoma was 52.26 years. These findings are comparable to those reported by Biswas et al[20]. and Abramowitz et al[21]. Increasing age has consistently been associated with increasing severity of cervical lesions because of prolonged exposure to oncogenic risk factors and persistent HPV infection.

The present study also demonstrated a significant association between higher parity and cervical carcinoma. Women with parity greater than three constituted the majority of malignant cases. Similar observations were reported by Fotara et al[22]. High parity is considered an important cofactor in cervical carcinogenesis because repeated cervical trauma during childbirth may increase susceptibility to HPV infection and neoplastic transformation.

Vaginal discharge was the most common presenting complaint in the present study, followed by irregular bleeding. However, postcoital bleeding and postmenopausal bleeding were more commonly associated with malignancy. Similar clinical presentations have been described in previous studies evaluating cervical lesions in Indian women[22].

Cervical cytology remains an important screening tool for early detection of premalignant and malignant lesions. In the present study, NILM was the most common cytological diagnosis, whereas LSIL, HSIL, and frank malignancy constituted smaller proportions of cases. The Bethesda System provided a standardized and clinically useful reporting framework for interpretation of cervical smears.

Histopathological examination revealed infection as the most common lesion, followed by dysplasia and malignancy. Squamous cell carcinoma was the predominant histological type identified in the present study, accounting for 92.1% of malignant lesions. Similar findings have been reported by Missaoui et al[23]. and Chaurasia et al[24]. The predominance of squamous cell carcinoma may be explained by the susceptibility of the transformation zone to persistent HPV infection and neoplastic change.

A major finding of the present study was the strong association between HPV infection and cervical malignancy. HPV positivity was detected in 97.36% of malignant lesions, which is comparable to findings reported by Bayo et al[10], Dybikowska et al[25], and Jung et al[9]. The prevalence of HPV in inflammatory lesions was significantly lower, supporting the etiological role of persistent high-risk HPV infection in cervical carcinogenesis.

HPV 16 was the predominant genotype identified in malignant lesions, followed by HPV 18. Similar observations have been reported by Muyden et al[8], Jung et al[9], and several international studies. Persistent infection with HPV

16 has consistently been associated with high-grade lesions and invasive carcinoma because of its high oncogenic potential.

The present study further demonstrated the usefulness of combined cytology, histopathology, and HPV DNA testing in evaluation of suspicious cervical lesions. Cytology serves as an effective screening tool, while histopathology remains the gold standard for definitive diagnosis. HPV DNA testing provides an objective and highly sensitive method for identifying high-risk infections and improves early detection when used in conjunction with conventional screening methods.

An important strength of the present study is that it simultaneously evaluated cervical cytology, histopathology, and HPV DNA status in women from Punjab using real-time PCR-based HPV detection. Very limited regional data are available correlating all these parameters together. The findings of the present study therefore contribute valuable information regarding HPV-associated cervical lesions in this population. The findings of the present study are consistent with contemporary evidence demonstrating the superior sensitivity of HPV testing over cytology for the early detection of cervical intraepithelial neoplasia and cervical cancer [26]. Recent international guidelines increasingly advocate primary HPV screening because persistent high-risk HPV infection is the principal etiological factor in cervical carcinogenesis [27]. The high sensitivity observed in the present study further supports the incorporation of HPV testing into organized cervical cancer screening programs.

From a public health perspective, HPV-based screening may contribute significantly to earlier detection of precancerous lesions, reduction in cervical cancer incidence, and achievement of global cervical cancer elimination targets. In resource-limited settings, combining HPV testing with cytological assessment may optimize diagnostic accuracy while maintaining cost-effectiveness and efficient utilization of healthcare resources[28,29].

However, the study had certain limitations. Being a hospital-based study, the findings may not fully represent the general population. Long-term follow-up of HPV-positive women was also not available. Further large-scale population-based studies are required to evaluate HPV prevalence, genotype distribution, and screening outcomes in Punjab.

Conclusions

Persistent infection with high-risk HPV plays a major role in cervical carcinogenesis. HPV 16 was the predominant genotype associated with malignant lesions in the present study. Increasing age and higher parity showed significant association with cervical malignancy.

Combined use of cervical cytology, histopathology, and HPV DNA testing improves identification of premalignant and malignant cervical lesions and may facilitate early diagnosis and timely management. The present study also highlights the need for strengthening cervical cancer screening programs and HPV awareness.

Funding

No funding sources.

Conflict of Interest

None declared.

References

1. Ellenson LH, Pirog EC. The female genital tract. In: Kumar V, Abbas AK, Aster JC (eds). Robbins and Cotran Pathologic Basis of Disease. 9th ed. Elsevier;2004:1001-4.
2. Path. Shaping a strategy to introduce HPV vaccines in India: Formative research results from the HPV vaccines: evidence for impact project. PATH;2009 [accessed on 2016 Nov 19]. Available from: www.rho.org/HPV-formative-research.htm .
3. Padburi VG and Daftary SN. Howkins and Bourne Shaw's Textbook of Gynaecology. 14th ed. Elsevier;2008:292-7.
4. Tavassoli FA, Devilee P. Tumours of the uterine cervix. In: World Health Organization classification of tumours. IARC;2003:259-90.
5. de Villiers, Fauquet C, Broker TR, Bernard HU, zur Hausen H. Classification of papillomaviruses. Virology. 2004;324:17-27.
6. Munoz N, Bosch FX, de Sanjose S, Herrero R, Castellsague X, Shah KV et al; International Agency for Research on Cancer Multicenter Cervical Cancer Study Group. Epidemiological classification of human papilloma virus types associated with cervical cancer. N Engl J Med. 2003;348(6):518-27.
7. Cullen AP, Reid R, Campion M, Lorincz AT. Analysis of the physical state of different human papilloma virus DNAs in intraepithelial and invasive cervical neoplasms. J Virol. 1991 Feb;65(2):606-12.
8. Muyden RC, ter Harmsel BW, Smedts FM, Hermans J, Kuijpers JC, Raikhlin NT et al. Detection and typing of human papilloma virus in Russian women: A prognostic study. Cancer 1999;85(9):2011-6.
9. Jung A, Cho NA, Lee SY, Kim IH, Lee C, Kim SJ et al. Correlation of cervical carcinoma and precancerous lesions with human papilloma virus (HPV) genotypes detected with HPV DNA chip microarray method. Cancer. 2003 Apr;97(7):1672-80.
10. Bayo S, Bosch FX, Sanjose D, Munco N, Cornbita AL, Coursaget P et al. Risk factors of invasive cervical cancer in Mali. Int J Epidemiol. 2002;31(1):202-9.
11. Kjaer SK, van den Brule AJC, Paull G, Svare EI, Sherman ME, Thomsen BL et al. Type specific persistence of high risk human papillomavirus (HPV) as indicator of high grade cervical squamous intraepithelial lesions in young women: population based prospective

ISSN 2583-2069

follow up study. BMJ 2002;325:572.
12. Koshial J, Lindsay L, Pimenta JM, Poole C, Jenkins D, Smith JS. Persistent human papilloma virus infection and cervical neoplasia: A systematic review and meta analysis. Am J Epidemiol. 2008;168(2):123-37.
13. Goldie SJ, Gaffikin L, Goldhaber-Fiebert JD, Gordillo-Tobar A, Levin C, Mahé C et al. Cost-Effectiveness of Cervical-Cancer Screening in Five Developing Countries.N Engl J Med. 2005;353:2158-216.
14. IARC. Screening tests. In: IARC Handbooks of cancer prevention. IARC;2005(10):59-110.
15. IARC. Effectiveness of screening in populations. In: IARC Handbooks of cancer prevention. IARC;2005(10):201-25.
16. Birdsong GG, Davey DD. Specimen adequacy. In: Nayar R, Wilbur DC (eds). The Bethesda System for Reporting Cervical Cytology. 3rd ed. Springer;2015:1-25.
17. IARC. Screening tests. In: IARC Handbooks of cancer prevention. IARC;2005(10):69-71.
18. Garland S, Tabrizi S. Methods for HPV detection: Polymerase chain reaction assays. In: Monsonego J (ed). Emerging issues on HPV infection: from science to practice. Krager;2006:63-72.
19. Petry KU, Menton S, Menton M, van Loenen-Frosch F, Gomes HC, Holz B et al. Inclusion of HPV testing in routine cervical cancer screening for women above 29 years in Germany: results for 8466 patients. British Journal of Cancer. 2003;88:1570-77.
20. Biswas LN, Manna B, Maiti PK, Sengupta S. Sexual risk factors for cervical cancer among rural Indian women: a case control study. Int J Epidemiol. 1997;24(3):491-5.
21. Abramowitz L, Guily JLS, Moyal-Barracco M, Jacquard AC, Largeron N, Dahlab A et al. Epidemiology, treatment pathways and costs of cancers potentially related to HPV infection in France. Value in Health. 2016 Nov;19(7):A347.
22. Fotara R, Gupta S, Gupta S. Sociodemograohic risk factors for cervical cancer in Jammu region of J and K state of India first ever report from Jammu. Indian J Sci Res. 2014;9(1):105-10.
23. Missaoui N, Hmissa S, Trabelsi A, Frappart A, Moncef, Mokni M et al. Cervix cancer in Tunisia: clinical and pathological study. Asian pacific J cancer prevention 2010;11:235-8.
24. Chaurasi R, Sharma P, Gharde P. A study of significance of mucin histochemistry in histopathological diagnosis of cervical carcinoma. Int J of Healthcare and Biomed Res. 2014 Jan;2(2):178-85.
25. Dybikowska A, Licznerski P, Podhajska A. HPV detection in cervical cancer patients in northern Poland. Oncol Rep. 2002;9(4):871-4.
26. Liang LA, Einzmann T, Franzen A, Schwarzer K, Schauberger G, Schriefer D, et al. Cervical cancer screening: comparison of conventional Pap smear test, liquid-based cytology, and human papillomavirus testing as stand-alone or cotesting strategies. Cancer Epidemiol Biomarkers Prev. 2021;30(3):474-484.
27. Arbyn M, Simon M, de Sanjosé S, Clarke MA, Poljak M, Rezhake R, et al. Accuracy and effectiveness of HPV mRNA testing in cervical cancer screening: a systematic review and meta-analysis. Lancet Oncol. 2022;23(7):950-960.
28. Oommen AM, Isaac R, Paul B, Weller D, Finkel ML, Thomas A, et al. Strategies for primary HPV test-based cervical cancer screening programme in resource-limited settings in India: results from a quasi-experimental pragmatic implementation trial. PLoS One. 2024;19(4):e0301385.
29. Campos NG, Perkins RB, Kinney W, Castle PE. Use of risk-based cervical screening programs in resource-limited settings. Cancer Epidemiol. 2023;84:102369.