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RESEARCH ARTICLE
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TO STUDY THE PREVALENCE, RISK FACTORS AND GENOTYPE DISTRIBUTION OF HUMAN PAPILLOMAVIRUS INFECTION AMONG WOMEN WITH AND WITHOUT INVASIVE CERVICAL CANCER ATTENDING A TERTIARY CARE CENTRE

Dr. Mashkoor Ahmad[1], Dr. Ramakant Tiwari[2], Dr. Mohammad Ali[3], Dr. Shoa Zehra[4]*, Dr Amit Kumar Singh[5]

Assistant Professor[1], Department of Radiation Oncology, Prasad Institute of Medical Sciences, Lucknow, Uttar Pradesh, India.
Assistant Professor[2], Department: Radiation Oncology, Sudha Medical College and Hospital, Kota, Rajasthan, India.
Assistant Professor[3], Department of Radiation Oncology, Hind Institute of Medical Sciences, Safedabad, Barabanki, Uttar Pradesh, India.
Senior Resident[4*], Department of Microbiology, King George's Medical University, Lucknow, Uttar Pradesh, India.
Assistant professor[5], Department of Microbiology, Prasad Institute of Medical Sciences, Lucknow, Uttar Pradesh, India.

***Corresponding Author:** Dr. Shoa Zehra
*Email ID: shoazehra926@gmail.com

ABSTRACT

Introduction: Human papillomavirus (HPV) is the name of a group of 200 known viruses. They do not cause concerns in most people, but infection with some high-risk types is common and can cause genital warts or cancer. Human papillomavirus (HPV) infection is a well-established cause of invasive cervical cancer (ICC).

Aim and Objective: To study the prevalence, risk factors and genotype distribution of human papillomavirus infection among women with and without invasive cervical cancer in women.

Material and Methods: A hospital-based study was conducted among 1126 women aged 21–78 years attending a tertiary cancer centre. Cervical samples were tested by cytology and HPV DNA real-time PCR, followed by genotyping. Sociodemographic and clinical variables were assessed.

Results: The overall prevalence of HPV infection was 37.3% (420/1126). Higher HPV positivity was noted in women with cytological abnormalities: 73.7% in ASC-H/HSIL and 92.6% in invasive squamous cell carcinoma, compared with 26.1% in NILM. Histologically confirmed ICC was observed in 17.2% (194/1126), with 95.2% (185/194) being HPV-positive. HPV16 was the most prevalent genotype (76.5%), followed by HPV18 (10.2%). Risk factors significantly associated with HPV infection included age >50 years, low socioeconomic status, illiteracy, high parity, and marital duration >10 years ($p<0.001$).

Conclusion: HPV infection, particularly HPV16, was highly prevalent among women with premalignant and malignant cervical lesions. These findings highlight the urgent need for widespread HPV vaccination and cervical cancer screening strategies in the region.

Keywords: Prevalence, Risk Factors, Genotype, Distribution, Human Papillomavirus, Invasive Cervical Cancer.

INTRODUCTION

Cervical cancer remains a major global health problem, ranking as the fourth most common cancer among women worldwide, with an estimated 604,127 new cases and 341,831 deaths in 2020【1】. Nearly 90% of these deaths occur in low- and middle-income countries (LMICs), where access to preventive measures such as screening and HPV vaccination is limited【2】. In India, cervical cancer continues to be the second most common malignancy among women, with approximately 123,907 new cases and 77,348 deaths reported in 2020【1】. Despite advances in prevention, the disease burden in India remains disproportionately high, reflecting gaps in public health infrastructure, awareness, and implementation of national vaccination programs【3】.

Persistent infection with high-risk human papillomavirus (HR-HPV) genotypes is a necessary cause of cervical cancer, being detected in 99.7% of invasive cervical carcinoma (ICC) cases globally【4】. Over 228 HPV genotypes have been identified, of which at least 15 are considered oncogenic, with HPV16 and HPV18 being the most dominant types associated with ICC【5,6】. Worldwide, these two types account for approximately 70% of all cervical cancers【7】. Other genotypes such as HPV31, 33, 45, 52, and 58 also contribute to regional variation in disease distribution【8】.

Epidemiological studies have demonstrated wide geographical differences in HPV prevalence and genotype distribution. The highest rates are seen in sub-Saharan Africa (24%) and Eastern Europe (21%), with lower but significant prevalence in South and Southeast Asia (14%)【9】. In India, HPV prevalence among women with normal cytology has been reported to vary from 9% to 36%, depending on region and population studied【10,11】. Studies consistently report HPV16 as the most common genotype, followed by HPV18, with minor contributions from other high-risk types【12–14】.

Socioeconomic and demographic factors such as low education, poverty, high parity, early marriage, and prolonged marital duration have been associated with increased risk of HPV infection and cervical cancer in India【15】. Rural women, in particular, are disproportionately affected due to poor access to healthcare facilities, cultural barriers, and lack of awareness regarding screening【16,17】.

HPV vaccination is a highly effective preventive strategy, and recent inclusion of HPV vaccines in India's universal immunization program marks an important step forward【18】. However, baseline data on genotype distribution are critical to guide vaccination and screening strategies tailored to regional needs. Prior Indian studies have highlighted substantial inter-state variability in HPV prevalence and genotypes【12,14,19】.

Therefore, this hospital-based study was designed to determine the prevalence, risk factors, and genotype distribution of HPV infection among women with and without invasive cervical cancer in women attending a tertiary care centre.

MATERIAL AND METHODS

This hospital-based, cross-sectional study was conducted at a tertiary cancer care centre over a period of 12 months i.e, June 2024 to June 2025. Women attending the outpatient and inpatient departments of gynecology and oncology were recruited after obtaining informed consent.

Study Population

A total of 1126 women aged 21–78 years were included. Women presenting for routine gynecological care, screening, or suspected cervical pathology were considered eligible.

Inclusion criteria: women aged ≥21 years, willing to provide cervical samples

Exclusion criteria: pregnant women, those with prior history of hysterectomy, prior pelvic radiotherapy, or inadequate/unsatisfactory cervical samples.

Data Collection
Sociodemographic and clinical details were collected through structured questionnaires and hospital records. Variables included age, socioeconomic status, education, marital duration, parity, and reproductive history.

Sample Collection and Cytology
Cervical exfoliated cells were collected using Ayre's spatula and cytobrush under aseptic precautions. Two smears were prepared from each sample:
1. Conventional cytology (Pap smear): Slides were fixed and stained by the Papanicolaou method and reported according to the Bethesda System (2014) into NILM, ASC-US, LSIL, ASC-H, HSIL, and invasive carcinoma.
2. HPV DNA testing: The remaining sample was preserved in transport medium for molecular analysis.

Histopathology
Women with abnormal cytology or suspicious clinical findings underwent colposcopy-directed biopsy. Histopathological examination was performed and categorized as benign, premalignant (CIN), or malignant (invasive cervical carcinoma).

HPV DNA Extraction and Detection
DNA was extracted from cervical cell specimens using a commercial extraction kit (Qiagen, Germany).
HPV DNA detection was performed using real-time PCR with primers targeting the L1 region.
Genotyping was conducted using a validated multiplex PCR-based assay capable of detecting at least 14 high-risk HPV genotypes (HPV16, 18, 31, 33, 35, 39, 45, 52, 56, 58, 59, and others). Positive and negative controls were included in each run.

Statistical Analysis Data were entered into Microsoft Excel and analyzed using SPSS version 25.0 (IBM Corp., USA). Categorical variables were expressed as frequencies and percentages, while continuous variables were expressed as mean ± SD. Associations between HPV infection and sociodemographic/clinical variables were tested using Chi-square or Fisher's exact test. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. A p-value of <0.05 was considered statistically significant.

RESULTS
A total of 1126 women aged 21–78 years were included in the study. The mean age was 45.6 ± 11.8 years. Most participants (889/1126; 78.9%) had been married for >10 years, while 237 (21.1%) had a marital duration of <10 years. The overall prevalence of HPV infection was 37.3% (420/1126).

Clinico-demographic characteristics and risk factors

HPV-positivity showed a strong association with several sociodemographic factors (Table I). Women aged >50 years had significantly higher infection rates compared to younger groups. Only 6 of 122 women (4.9%) aged <30 years were HPV-positive, whereas 171 of 375 women (45.6%) aged 50–65 years and 17 of 32 women (53.1%) above 65 years were HPV-positive (p<0.001).

Illiteracy and low socioeconomic status were also associated with higher HPV-positivity, with infection rates of 40.8% (297/728) in illiterate women compared to 30.9% (123/398) in literate women. Similarly, women belonging to low/middle socioeconomic class had a significantly higher HPV prevalence (41.2%; 387/940) than those from higher class (17.7%; 33/186; p<0.001).

HPV infection correlated strongly with marital duration and parity. Women married for >10 years had nearly six times higher infection rates (41.6%; 370/889) compared to those married for <10 years (20.7%; 49/237). Similarly, higher parity (>2 children) was associated with 43.3% positivity (339/783) compared to 23.6% among those with ≤2 children (81/343). Hindu women had significantly higher positivity (40.4%; 398/986) compared to women of other religions (15.7%; 22/140).

Table I. Sociodemographic variables in relation with HPV status

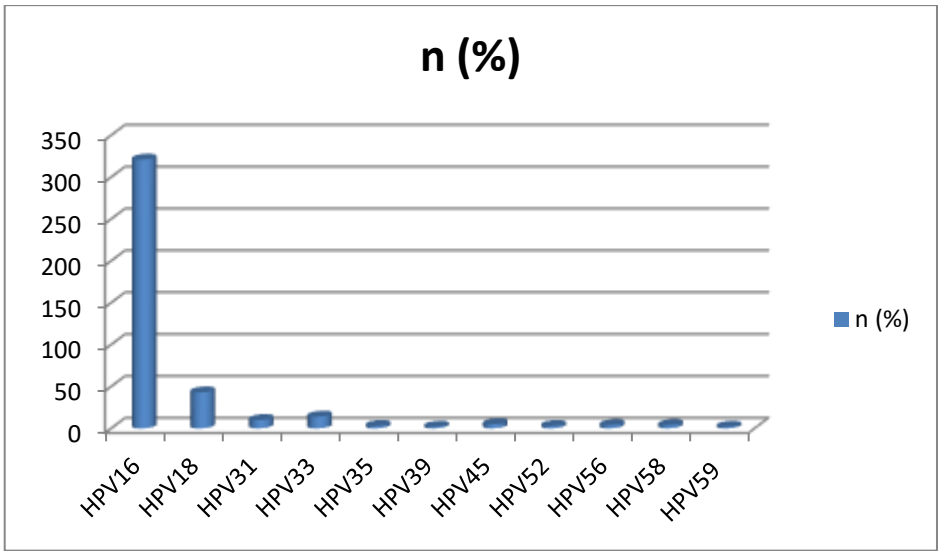
Variable	Total (n=1126)	HPV+ (n=420)	HPV– (n=706)	OR (95% CI)	p-value
Age					
<30 yrs	122	6	116	-	<0.001
30–50 yrs	597	226	371		
>50–65 yrs	375	171	204		
>65 yrs	32	17	15		
Socioeconomic status					
Low/Middle	940	387	553	3.05 (2.16–4.32)	<0.001
High	186	33	153		
Education					
Illiterate	728	297	431	1.61 (1.28–2.02)	<0.001
Literate	398	123	275		
Married life for					
<10 yrs	237	49	188	2.7 (1.99–3.65)	<0.001
>10 yrs	889	370	519		
Parity					
<2	343	81	262	2.49 (1.93–3.21)	<0.001
>2	783	339	444		

Table II. Correlation of HPV positivity with cytology and histopathology (n=1126)

Variable	Total	HPV16	HPV18	Other strains	>1 strain	HPV+	HPV–
Cytology (PAP)							
NILM	734	134	29	27	2	192	542
ASCUS	81	11	1	4	1	17	64
LSIL	43	2	0	1	0	3	40
ASC-H	11	6	1	2	1	10	1
HSIL	88	54	3	5	2	64	24
SCC	94	76	5	4	2	87	7
Neuroendocrine	1	1	0	0	0	1	0
Unsatisfactory	74	39	4	5	1	49	25
Histopathology							
Benign/Pre-malignant	265	134	19	31	2	186	79
Malignant (ICC)	194	151	17	12	5	185	9

Table III. Prevalence of HPV genotypes (n = 420 HPV+)

Genotype	n (%)
HPV16	321 (76.5)
HPV18	43 (10.2)
HPV31	10 (2.4)
HPV33	14 (3.3)
HPV35	3 (0.7)
HPV39	2 (0.5)
HPV45	5 (1.2)
HPV52	3 (0.7)
HPV56	4 (0.9)
HPV58	4 (0.9)
HPV59	2 (0.4)
Multiple strains	8 (1.9)



Graph No. 1: Graphical Representation of Genotype

Table IV. HPV genotype distribution by age group

Genotype	<30 yrs	30–40 yrs	40–50 yrs	>50 yrs
HPV16	5	33	135	148
HPV18	0	7	19	17
HPV31	0	3	5	2
HPV33	1	2	5	6
HPV45	0	2	3	0
HPV52	0	1	1	1
HPV58	0	0	2	2
Others	0	4	2	5
Multiple	0	2	4	2

Cytological findings

Cytology revealed that 734 women (65.2%) were negative for intraepithelial lesion or malignancy (NILM), while 124 (11%) had ASCUS/LSIL, 99 (8.8%) had ASC-H/HSIL, and 95 (8.4%) were diagnosed with invasive squamous cell carcinoma (SCC), including one neuroendocrine carcinoma. An unsatisfactory report was recorded in 74 (6.6%) women.

HPV-positivity correlated significantly with cytological abnormality ($p<0.001$; Table II). While only 26.1% (192/734) of NILM cases were HPV-positive, positivity rose to 15.3% (19/124) in ASCUS/LSIL, 73.7% (73/99) in ASC-H/HSIL, and 92.6% (88/95) in SCC cases. Notably, the single neuroendocrine carcinoma also tested positive for HPV.

Histopathological findings

Biopsies were performed in 523 women, of which 194 (17.2%) were confirmed cases of invasive cervical cancer (ICC). Among these, 191 were squamous cell carcinoma, 2 adenocarcinoma, and 1 neuroendocrine carcinoma. HPV infection was detected in 95.2% (185/194) of confirmed ICC cases, with only 9 women testing negative.

In comparison, benign and premalignant lesions such as cervicitis, metaplasia, and CIN showed an overall positivity of 70.2% (186/265).

HPV genotype distribution

Of the 420 HPV-positive women, genotyping identified HPV16 as the most prevalent genotype (76.5%; 321/420), followed by HPV18 (10.2%; 43/420). Other high-risk types included HPV33 (3.3%), HPV31 (2.4%), HPV45 (1.2%), HPV56 (0.9%), HPV58 (0.9%), HPV35 (0.7%), HPV52 (0.7%), HPV39 (0.5%), and HPV59 (0.4%). Multiple genotype infections were found in 1.9% (8/420) of cases (Table III).

Genotype distribution varied with age (Table IV). HPV16 was most common across all age groups, peaking in women >50 years (148 cases). HPV18 was more common in women aged 30–50 years, while HPV33 and HPV31 showed a more even spread across middle and older age groups. Multiple infections were rare across

DISCUSSION

The present hospital-based study among 1126 women provides important insights into the prevalence, risk factors, and genotype distribution of human papillomavirus (HPV) infection in India. We observed an overall HPV prevalence of 37.3%, which is higher than the pooled prevalence of 9–36% reported in prior Indian studies among women with normal cytology【10–14】. This difference may be attributed to the hospital-based nature of our study, with many participants presenting with gynecological symptoms or suspected pathology, thereby representing a higher-risk population.

Our findings confirm HPV16 as the most prevalent genotype (76.5%), followed by HPV18 (10.2%). These results align with large multicentric studies from India and globally, which consistently report HPV16 as the dominant type in invasive cervical carcinoma (ICC), accounting for up to 70% of cases【7,12,13】. The predominance of HPV16 is clinically significant, as it has greater oncogenic potential compared to other high-risk genotypes【6,8】. Notably, we found only 1.9% of cases with multiple HPV infections, much lower than reports from sub-Saharan Africa and Latin America, where coinfections are more common【9】. This suggests regional variability in HPV transmission dynamics.

In our study, HPV positivity showed a strong correlation with cytological and histopathological abnormalities. While only 26.1% of NILM cases were HPV-positive, the prevalence increased to 92.6% in squamous cell carcinoma. This observation reinforces the causal association between persistent high-risk HPV infection and cervical carcinogenesis【4】. Similar patterns have been described in meta-analyses, where HPV was detected in over 95% of ICC cases worldwide【7】.

Several sociodemographic factors emerged as significant predictors of HPV infection. Women aged >50 years, those with higher parity, low literacy, low socioeconomic status, and longer marital duration had significantly higher infection rates. These findings are in agreement with previous

Indian studies highlighting the influence of poverty, illiteracy, and early marriage on HPV transmission and cervical cancer risk【15–17】. Such associations underscore the need for context-specific interventions focusing on education, awareness, and improved access to screening and vaccination in underserved communities.

The age-specific distribution of genotypes in our study revealed that HPV16 was the most frequent type across all age groups, with peak prevalence in women above 50 years. HPV18 infections were more common in women aged 30–50 years. This is consistent with the natural history of HPV, where persistence of high-risk genotypes increases with age, and clearance rates decline【9】. These trends have important implications for screening programs, as older women remain at significant risk for HPV-associated malignancy.

Our results reinforce the urgent need for strengthening HPV vaccination and cervical cancer screening strategies in India. Recent inclusion of the HPV vaccine in India's universal immunization program is an encouraging step【18】. However, genotype surveillance studies like ours are essential to monitor regional variations and guide vaccine policies. For example, nonavalent vaccines covering HPV31, 33, 45, 52, and 58 could offer broader protection in the Indian context【12,14】.

Recent studies from 2024 have highlighted the increasing importance of integrating HPV vaccination with organized screening programs, particularly in low- and middle-income countries. A multicentric Indian study reported that while HPV16 continues to dominate as the leading genotype, there is a gradual emergence of other oncogenic strains such as HPV31 and HPV33, suggesting the potential benefit of nonavalent vaccines in the region【20】. Moreover, the study reaffirmed the strong association of HPV positivity with sociodemographic risk factors, particularly among older women and those from low socioeconomic strata, consistent with our findings【21】.

In 2025, evidence further emphasized that the inclusion of HPV vaccines in national immunization programs is beginning to show an impact on reducing the prevalence of high-risk HPV infections in adolescent and young adult women【22】. However, challenges remain in achieving adequate coverage due to vaccine hesitancy, affordability, and healthcare access gaps. These data support the urgent need to expand both vaccination and screening efforts to ensure equitable cervical cancer prevention strategies across diverse populations.

CONCLUSION

Strong associations were observed with sociodemographic risk factors, particularly low education, poverty, multiparity, and advanced age. The findings underscore the etiological role of HPV in cervical cancer and highlight the urgent need for comprehensive preventive strategies, including universal HPV vaccination, awareness programs, and robust cervical cancer screening in high-risk populations.

Limitation of the study

1. Cross-sectional design limits the ability to establish temporal relationships between HPV infection and disease progression.
2. Only high-risk HPV genotypes were included in the genotyping assay; low-risk types such as HPV6 and HPV11, which are relevant for genital warts, were not assessed.
3. Behavioral risk factors such as smoking, sexual history, and partner-related variables were not fully explored, which could provide additional insights into HPV transmission dynamics.
4. Longitudinal follow-up to assess persistence and clearance of HPV infection was not performed.

DECLARATIONS:

Conflicts of interest: There is no any conflict of interest associated with this study

Consent to participate: There is consent to participate.
Consent for publication: There is consent for the publication of this paper.
Authors contributions: Author equally contributed the work.

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