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The Impact of Human Papilloma Virus Genotype on Clinical Response to Chemoradiotherapy in Patients of Carcinoma Cervix

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Abstract

Aim and Objective-Cervical cancer ranks as the fourth most common cancer and cause of cancer-related deaths in women worldwide. In India, it is the second most common cancer among women, with 123,907 new cases and 77,348 deaths reported in 2020, contributing significantly to global incidence and mortality rates.Global studies have consistently shown that over 99% of cervical cancer cases are associated with the presence of the Human Papillomavirus (HPV). This study was aimed to study the impact of HPV genotype on clinical response to chemoradiotherapy and to elucidate the correlation of HPV genotype in patients of carcinoma cervix with age, stage and histopathology.

Materials and Methods:This study included 46 patients with biopsy-confirmed carcinoma cervix, who had an ECOG[17] performance status of 0-2 and were classified as FIGO stages IIB to IIIC2. At baseline, patients underwent a comprehensive evaluation, including blood tests, CECT whole abdomen or CEMRI pelvis scans and a detailed clinical history and physical examination. Cervical swabs were also collected to assess HPV genotype, including the presence or absence of HPV and identification of 14 high-risk HPV genotype using Real-Time PCR kits. The treatment regimen consisted of external beam radiation therapy with concurrent chemotherapy, comprising weekly cisplatin injections at 40 mg/m², followed by brachytherapy. Following treatment, patients were followed up at first, third and sixth months with CECT whole abdomen or CE MRI pelvis scans, which were compared to baseline scans using RECIST criteria to assess treatment response, categorized as good or poor. Chi Square test of significance was used for all the calculations.

Results- Among 46 patients, 45 (97.8%) were HPV-positive and 1 was HPV-negative(2.2%). Squamous cell carcinoma (SCC) was the predominant histology across all age groups.The treatment response to chemoradiotherapy was good in 37 patients (80.4%) and poor in 9 patients (19.6%), irrespective of HPV status. The difference in treatment response between HPV-positive and HPV-negative patients was not statistically significant (P = 0.546). Out of 46 patients, 31.1% had HPV 16 as a single genotype, 4.3%

had HPV 18, and 41.3% had multiple genotypes including HPV 16 and 18. Additionally, 13% had single or multiple genotypes other than HPV 16 and 18, including HPV 33, 66, 56, and 58 and one patient negative for HPV. At a significance level of α=0.05, the null hypothesis cannot be rejected for HPV status (p=0.466 > 0.05). This suggests insufficient evidence to establish a significant association between treatment response and HPV status and warranting further investigation into its role in cervical carcinoma.

Conclusion- This study highlights the importance of HPV status in predicting treatment response to chemoradiotherapy in cervical cancer. HPV-positive tumors showed better outcomes, but HPV genotype had no significant impact on treatment response. Further research is needed to confirm these findings and explore the role of HPV subtypes in cervical carcinoma

Keywords: Carcinoma cervix, Human Papilloma Virus, HPV Genotype, Carcinoma cervix chemoradiotherapy, Treatment Response

1. INTRODUCTION

Cervical cancer remains a significant global health challenge, particularly in low and middle income countries with limited access to preventive measures and healthcare resources. Despite substantial advancements in medical science and technology, cervical cancer continues to exert a significant toll on women's health and well-being worldwide. It is the fourth most common cancer and cause of cancer-related deaths in women globally[1]. In India, cervical cancer is the second most common cancer among women, with 123,907 new cases and 77,348 deaths reported in 2020, making it the leading contributor to global incidence and mortality rates[2]. Persistent infection with human papilloma virus (HPV) is the primary cause of cervical cancer[3]. HPV is a non-enveloped, double-stranded DNA virus that primarily infects epithelial cells of the skin and mucous membranes, with over 200 known genotypes[4].Human papilloma virus (HPV) produces 8 to 10 proteins, with E6 and E7 interacting with cellular p53 and pRB proteins. This disrupts their normal functions and alters cell cycle regulation, leading to increased and sometimes abnormal mitotic events, a hallmark of both pre-malignant and malignant conditions[5].

High-risk HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68), probably high-risk-HPV types (26, 53, 66, 70, 73, and 82) and low-risk-HPV types (6, 11, 40, 42, 43, 44, 54, 61, 62, 67, 81, 83, 89). Additional epidemiological risk factors linked to cervical cancer include a history of smoking, parity, oral contraceptive usage, early initiation of sexual activity, higher number of sexual partners, history of sexually transmitted diseases, specific autoimmune conditions, and chronic immune suppression[6.] Concurrent chemoradiotherapy (CTRT) with cisplatin-based chemotherapy is the standard treatment[7]. The combination of external beam radiotherapy (EBRT) with concurrent chemotherapy followed by intracavitary brachytherapy (ICBT) improves treatment outcomes and reduces the risk of residual disease or recurrence. Gupta R et al. studied the correlation between HPV infection and treatment response in cervical carcinoma patients. Using Real-Time PCR, 42 HPV-positive cases (67% HPV 16, 21% HPV 18) and 8 HPV-negative cases. HPV-positive tumors showed better treatment response (p=0.019) compared to HPV-negative tumors. Poor radiotherapy response was observed in HPV-negative patients and those positive for HPV 18[8]. Mamiko Onuki et al. conducted a study on the correlation between HPV genotype and prognosis in cervical cancer patients undergoing radiotherapy, results indicated that HPV 16 positive genotype was a favorable prognostic factor for patients with cervical cancer at FIGO[18] stages III and IV (p=0.06)[9]. Harima Y et al. studied the correlation between

HPV genotypes and survival in cervical carcinoma patients, finding that HPV-negative patients had significantly shorter survival compared to HPV-positive patients[10]. A study by Nakagawa et al. compared the prognosis of HPV-positive and HPV-negative cervical cancer patients, concluding that HPV 18 was associated with a poorer prognosis than HPV 16[11.] This study conducted for elucidate the correlation of HPV genotype in patients of carcinoma cervix with age, stage and histopathology and to study the impact of HPV genotype on clinical response to chemoradiotherapy in patients of carcinoma cervix.

2. Materials And Methods

This was a single tertiary care institution, observational cohort study of 46 patients of locally advanced carcinoma cervix conducted for a duration of 18 months, from October 2022 to March 2024, to assess the impact of HPV genotype on clinical response to chemoradiotherapy in patients of carcinoma cervix at Vardhman Mahaveer Medical College and Safdarjung Hospital. The study was approved by the Institutional Ethical Committe. Written and informed consent was taken from each patient. After a detailed clinical history and examination, histopathological confirmed cases of carcinoma cervix in Indian population, age more than 18 year with Eastern Cooperative Oncology Group (ECOG)[17] status 0-2 having FIGO[18] Stage IIB to Stage lllc2 of carcinoma cervix were selected for the study. Patients who received any chemotherapy or radiotherapy treatment in the past or had recurrent or metastatic disease or second primary were excluded. The primary endpoint of the study was to evaluate the impact of HPV genotype on clinical response to CCRT in the patients of carcinoma cervix using RECIST[19] criteria 1.1 The secondary endpoint was to elucidate the correlation of HPV genotype in patients of carcinoma cervix with age, stage and histopathology. Follow up done at first, third and sixth months post treatment completion.

Treatment

Each participant was inquired with detailed clinical history(Socioeconomic status, sexual behavior, reproductive history, contraceptive use, hygiene, history of STIs, and cervical screening practices) and thorough examination, including general, systemic, and local assessments (per vaginal, abdominal, and rectal) were conducted to evaluate the primary tumor, its extent and regional lymph nodes. Baseline investigations included complete blood count, liver and kidney function tests, serum electrolytes, chest X-ray (PA view), HPV genotyping, and baseline imaging studies like CECT whole abdomen and/or MRI pelvis. For HPV genotyping Cervical cells were collected with the help of sterile transport cotton swab sticks which was placed in transport media (normal saline) and was send to molecular laboratory, where HPV DNA extraction and genotype was detected by using Real time PCR DNA kit - TRUPCR test kit ,which detected HPV high risk (14 types- HPV 16, 18, 21. 33. 35, 45, 51, 52, 56, 58, 59, 66, 68). External beam radiotherapy (EBRT) was delivered using a Cobalt-60 unit, with individualized treatment planning for each patient. A pelvic dose of 50.4 Gray (Gy) was administered using either the two-field parallel-opposed technique (anterior/posterior field) or the four-field box technique, delivered in 28 fractions over 5 weeks and 3 days (Monday to Friday). If indicated, the para-aortic dose deliverd 45 Gy in 25 fractions over 5 weeks using extended field radiation therapy (EFRT). Concurrent chemotherapy with cisplatin (40 mg/m²) was administered to all patients during EBRT. Weekly per vaginum examinations, complete blood counts, and renal function tests were performed throughout the EBRT course. Approximately one week after completing EBRT, all patients underwent high-dose-rate brachytherapy using intracavitary applicators. Three, weekly fractions were delivered, each providing a

dose of 7–7.5 Gy at point A. All study participants were followed up at 1, 3, and 6 months post-chemoradiotherapy, with responses assessed using RECIST 1.1[19] criteria and categorized as complete response (CR), partial response (PR), progressive disease (PD), or stable disease (SD), as detailed in the annexure. If Complete response (no residual disease) was considered an overall good response, while progressive disease, partial response, stable disease or death were classified as poor responses as seen on clinical examination and follow up imaging scans. Descriptive analysis was carried out by frequency and percentage for categorical variables. Continuous variable was presented as mean ± SD. Chi Square test of significance was used to estimate impact of HPV genotype on clinical response to chemoradiotherapy in patients of carcinoma cervix ,$p<0.05$ was considered significant.

3. RESULTS

The present study was designed to study the impact of HPV genotype on clinical response to chemoradiotherapy and to elucidate the correlation of HPV genotype in patients of carcinoma cervix with age, stage and histopathology. In a studied population of 46 patients, the age distribution revealed that 13.0% were aged 18–39 years, 71.7% were 40–59 years, and 15.2% were over 60 years, with a mean age of 50.5 years (standard deviation: 8.23). The youngest patient was 35 years old, and the oldest was 67 (Table 1). Regarding histological variation, 8.7% (n=4) of patients had adenocarcinoma histology, while 91.3% (n=42) had squamous cell carcinoma (SCC), making SCC the predominant type (Table 1). Among studied population, FIGO[18] staging showed that stage II B was the most common (41.3%), followed by stage III C1 (37%), stage III B (17.4%), and stage III C2 (4.3%). DNA PCR analysis identified 14 High risk HPV genotype. In the present study 45 (97.8%) out of 46 patients were positive for HPV infection and 1 case negative for HPV infection (HPV-independent carcinoma cervix) was found in individuals aged more than 60 and constituting 2.2% of the total study population (n=46) (Table 1). HPV 16 was detected in 31.1% of cases as single genotype, HPV 18 alone in 4.3% cases as single genotype, presence of HPV Multiple positive HPV sub genotype included HPV 16 &18 (HPV16,18,52,58,56,66,58,68,31,33) detected in 41.3% of HPV positive patients(N=19) and Presence of Single/Multiple HPV genotype (other than HPV 16 &18) included HPV 33(N=3), HPV 66 (N=2) & HPV 56,58 (N=1) constituted about 13% (n=6) cases in studied population(n=46).(figure 1)

Figure1: HPV genotype distribution in the study population (N=46)

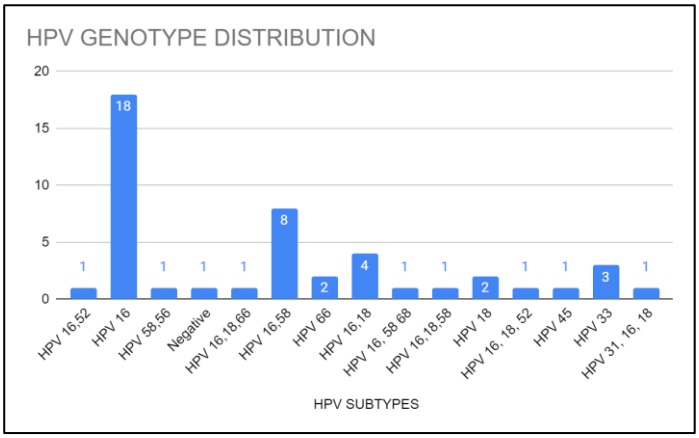

Table 1: Baseline and treatment characteristics of the study population (N=46)

Variables	Frequency	Percentage
Age group		
<40 years	6	13.0%
40 to 59 years	33	71.7%
>=60 years	7	15.2%
Stage		
IIB	19	41.3%
IIIB	8	17.4%
IIIC1	17	37.0%
IIIC2	2	4.3%
Histopathology		
Adenocarcinoma	4	8.7%
SCC	42	91.3%
HPV Infection		
Present/HPV Positive	45	97.8%
Absent/HPV Negative	01	2.2%
HPV genotype		
Single genotype HPV 16 positive	18	39.1%
Single genotype HPV 18 positive	2	4.3%
Single/multiple HPV positive genotype (other than 16&18)- 33,66,56,58	6	13.0%
Multiple positive HPV genotype included HPV 16&18	19	41.3%
HPV negative genotype	1	2.2%
Treatment Response		
Good	37	80.4%
Poor	9	19.6%

Co-Relationship between HPV Genotype and Age, Stage and Histopathology

In the studied population, the majority (71.7%, n=33) were aged 40–59 years, while 13% (n=6) were under 40, and 15.2% (n=7) were aged 60 and above. HPV genotype positivity was observed in 97.8% (n=45) of patients, with a single HPV-negative case (2.2%, n=1). HPV 16 was the predominant single genotype, present in 40% (n=18) of HPV-positive cases, while multiple HPV genotypes (HPV-16, 18, 52, 58, 56, 66, 58, 68, 31, 33)) were detected in 41.3% (n=19). A single HPV 18 genotype was most common in the 40–59 age group (6%). Rare genotype including HPV 33 (n=3), HPV 66 (n=2), and HPV

56,58 (n=1), constituted 13% of cases across age groups. HPV-independent carcinoma was identified in one case (2.2% overall, 14.28% in the age above 60 years).(Table 2)

Out of 46 patients, 45 were HPV-positive, indicating a high prevalence of HPV infection. HPV 16 was the most common genotype, found in 18 cases, while HPV 18 was detected in 2 cases. Single/multiple genotypes other than HPV 16 and 18 were observed in 6 cases, and multiple HPV genotypes, including HPV 16 & 18, were identified in 19 cases. All 42 patients with SCC were HPV-positive, with HPV 16 detected in 18 cases, HPV 18 in 2 cases, other genotypes in 5 cases, and multiple HPV genotypes (16 & 18) in 17 cases. Among 4 adenocarcinoma cases, 3 were HPV-positive, with 1 showing other genotypes and 2 exhibiting multiple genotypes (16 & 18). SCC was predominantly associated with HPV, with HPV 16 being the most prevalent across both SCC and adenocarcinoma. Multiple HPV genotypes were more frequent in SCC, highlighting the complexity of HPV's role in cervical carcinogenesis.(Table 2)

Among the 46 patients analyzed, most were diagnosed at stage IIB (41.3%), followed by IIIC1 (36.9%), IIIB (17.4%) and IIIC2 (4.3%). HPV positivity was nearly universal across all stages (97.8%), with HPV 16 being the most prevalent subtype, found in 40% of HPV-positive cases across all stages.(Table 2)

Table 2: Co-Relationship between HPV Genotype and Age, Stage ,Histopathology, Treatment Status and response to chemoradiotherapy.

Variables	**Number of patients**	**HPV Positive**	**HPV Negative**	**Single genotype HPV 16 positive**	**Single genotype HPV 18 positive**	**Single/multiple HPV positive genotype (other than 16&18)**	**Multiple positive HPV genotype included HPV 16&18**
Age group							
<40 years	6	6	0	2	0	2	2
40 to 59 years	33	33	0	15	2	1	15
>=60 years	7	6	1	1	0	3	2
Total	46	45	1	18	2	6	19
FIGO Stage							
IIB	19	19	0	7	0	1	11
IIIB	8	7	1	1	2	2	2
IIIC1	17	17	0	9	0	3	5
IIIC2	2	2	0	1	0	0	1
Total	46	45	1	18	2	6	19
Histopathology							
Adenocarcinoma	4	3	1	0	0	1	2
SCC	42	42	0	18	2	5	17
Total	46	45	1	18	2	6	19
Treatment Status							

Complete	38	37	1	14	2	5	16
Incomplete	8	8	0	4	0	1	3
Total	46	45	1	18	2	6	19
Response							
Good	37	36	1	14	2	5	15
Poor	9	9	0	4	0	1	4
Total	46	45	1	18	2	6	19

Relationship between HPV Infection Status and response to radiotherapy In our study, 80% (n=36) of the 45 HPV-positive cervical cancer patients showed a good response to chemoradiotherapy, while 20% (n=9) had a poor response including local recurrence, residual disease, distant metastasis, or death. This demonstrates that most HPV-positive patients responded favorably to treatment, with a low incidence of adverse outcomes. Similarly, the single HPV-negative patient also demonstrated a good response to chemoradiotherapy. The difference in treatment response between HPV-positive and HPV-negative patients was not statistically significant (P = 0.546). (Table 3)

Table 3. Relationship between HPV Status and response to radiotherapy

HPV Genotype	Good Response	Poor Response	P Value
HPV Positive	**36**	**9**	**0.546**
HPV Negative	**1**	**0**	

Relationship between HPV Sub types and response to radiotherapy

Out of 46 patients, 91.3% (n=42) completed External Beam Radiation Therapy (EBRT), while 8.7% (n=4) did not, due to reasons such as personal exigencies, brain metastasis (1 case), or death during CCRT (1 case). Among the 42 patients who completed EBRT, 38 proceeded to brachytherapy, with 10.5% (n=4) not completing it. Ultimately, 82.6% (n=38) of the study population completed the standard treatment (both CCRT and brachytherapy), while 17.4% (n=8) did not. Among those who completed treatment, 97.37% (n=37) were HPV-positive, and 1 patient was HPV-negative. In the incomplete treatment group (n=8), all were HPV-positive, with 4 cases having HPV 16 genotype, 1 case having other HPV genotype, and 3 cases showing multiple genotype, including HPV 16 and 18.(Table 2)

The first follow-up at first month post treatment completion assessment through RESIST 1.1[17] criteria among 46 enrolled patients showed a Complete Response (CR) in 67.4% (n=31), Partial Response (PR) in 19.6% (n=9), Stable Disease in 4.3% (n=2), Progressive Disease (PD) in 2.2% (n=1), and death in 6.5% (n=3). By the second follow-up at third month post completion of treatment among all enrolled patients CR increased to 78.3% (n=36), while PR was 8.7% (n=4), PD 4.3% (n=2), and death 8.7% (n=4). At the third follow-up at sixth month post treatment completion, CR reached 80.4% (n=37), PR 6.5% (n=3), PD 2.2% (n=1), and death 10.9% (n=5). Overall, 80.4% (n=37) achieved CR, indicating a good response, while 19.5% (n=9) experienced PR, PD, or death, reflected a poor response to chemoradiotherapy irrespective of HPV Genotype.(Table 4)

Among the 37 patients with an overall good response during follow-ups, 44.4% (n=14) were positive for HPV 16, 5.4% (n=2) for HPV 18, and 5.4% (n=2) for HPV 33. Additionally, 10.8% (n=4) were positive for both HPV 16 and 18, 2.7% (n=1) for HPV 16 and 52, 2.7% (n=1) for HPV 58 and 56, and 2.7% (n=1) for HPV 16, 18, and 66. Other combinations included 16.2% (n=6) positive for HPV 16 and 58, 5.4%

(n=2) for HPV 66, 2.7% (n=1) for HPV 16, 18, and 58, 2.7% (n=1) for HPV 45, and 2.7% (n=1) for HPV 16, 18, and 31, with one patient (2.7%) testing HPV-negative. Among the 9 patients with an overall poor response, 44.4% (n=4) were positive for HPV 16, 11.1% (n=1) for both HPV 16 and 18, 11.1% (n=1) for HPV 33, 11.1% (n=1) for HPV 16, 58, and 68, and 11.1% (n=1) for HPV 56 and 58. At a significance level of α=0.05, the null hypothesis cannot be rejected for HPV status ($p=0.466 > 0.05$). This suggests insufficient evidence to establish a significant association between treatment response and HPV status.(Table 3)

Table 4: Follow ups and response assessment using RESIST 1.1 Criteria

N=46	**Good Response**	**Poor Response**			
	CR Cases	PR Cases	Stable disease	PD Cases	Death Cases
At First follow up	31	9	2	1	3
At Second follow up	36	4	0	2	4
At Third follow up	37	3	0	1	5

4. DISCUSSION

In our study group, the mean age was 50.5 years (SD: 8.23), with ages ranging from 35 to 67 years. Similarly, Gupta et al. reported a mean age of 49.2 years, with most patients aged 40-59 years[8]. Das et al. also found that cervical cancer cases in India are most common in individuals aged 45-60 years[12], with some studies reporting an even distribution between ages 30-39 and 60-69 years. This trend is influenced by factors like early sexual activity (leading to earlier HPV infection) and active Pap screening in developed countries, enabling earlier detection compared to developing nations like ours, where poor awareness and compliance delay diagnosis at premalignant or early stages.

In our study, 91.3% (42/46) of cervical cancer cases were squamous cell carcinoma (SCC), while 8.7% (4/46) were adenocarcinoma. Similarly, Gupta et al. reported SCC in 96% and adenocarcinoma in 4% of cases[8]. Shukla et al. also found 10-15% of cases to be adenocarcinoma, reinforcing that SCC is the predominant histological type, with adenocarcinoma representing a smaller proportion[13]. In our study of 46 cases, FIGO[18] staging distribution was as follows: Stage IIB (41.3%), Stage IIIC1 (37%), Stage IIIB (17.4%), and Stage IIIC2 (4.3%). Most cases were in Stage IIB, followed by Stage IIIC1 and IIIB, with fewer in Stage IIIC2. Similarly, Gupta et al. reported 24% in Stage II and 76% in Stage III[8]. Munirajan's study in India also found 83% of tumors in Stage III and 14% in Stage II[14]. In contrast, Nakagawa's study from Western countries reported 73.9% of cases in early stages and only 21% in Stage III[11]. Late-stage presentations in developing countries, including ours, are linked to low socioeconomic status and limited health awareness among women. In our study, 97.8% (45/46) of cases were positive for HPV genotypes. HPV 16 was found in 31.1%, HPV 18 alone in 4.3%, and HPV 16 & 18 with other sub types in 41.3%. Other sub types accounted for 13% of cases. Gupta et al. reported HPV 16 in 67%, HPV 18 in 21%, and other sub types, including HPV 45 and 33, in smaller proportions. Similarly, Maniranjan et al. detected HPV DNA in 70% of cases, with HPV 16 in 53%, HPV 18 in 13.3%, and HPV 33 in 3.3%. In contrast, Hariharan et al. observed HPV 16 (66.7%) and HPV 18 (19.4%) as the predominant types in rural Hyderabad, along with other sub types. Advances in detection techniques with improved specificity

and sensitivity have reduced false negatives, contributing to these findings.As the kits can only detect high risk HPV Genotype sub types could be a limitation for HPV independent cancer detection.5In our study, 2.2% (1/46) of cases were HPV-negative (HPV-independent). Literature suggests various reasons for HPV-independent cervical carcinoma. In contrast, Gupta et al. reported 16% (8/50) HPV-negative cases. This variation may be attributed to the higher sensitivity of the HPV DNA PCR kits used in our study.But our HPV testing kits only limited for high risk genotype detection.6In our study, most patients were diagnosed at Stage IIB (41.3%), followed by IIIC1 (36.9%), IIIB (17.4%), and IIIC2 (4.3%). HPV positivity was nearly universal (97.8%), with HPV 16 being the most common subtype across all stages (40%). Similarly, Gupta et al. reported HPV 16 in 70% of Stage II cases and 65% of Stage III cases[8]. No significant variation in HPV genotype distribution was observed across stages ($p = 0.55$), indicating consistency in HPV subtype prevalence regardless of disease stage. In our study, all SCC cases (42/42) were HPV-positive, while 75% (3/4) of adenocarcinoma cases tested positive, with one HPV-negative adenocarcinoma. Among the 40 HPV-positive SCC cases, 42.8% were HPV 16, 4.7% HPV 18, and 3.71% had other HPV sub types. In comparison, Gupta et al. reported 48 SCC cases, with 40 HPV-positive (67.5% HPV 16, 20% HPV 18, and others)[8]. These findings highlight variations in HPV genotype distribution. Similarly, Das et al. found HPV 16 to be the most prevalent type in both SCC and adenocarcinoma in India, differing from global trends where HPV 18 is more common in adenocarcinoma[12]. In our study, 80% (36/45) of HPV-positive patients showed a good response to radiotherapy, while 20% (9/45) experienced poor outcomes, including recurrence, residual disease, metastasis, or death. The sole HPV-negative patient also showed a good response, but the small sample size limits conclusions about HPV-negative cases. Gupta et al. reported 69.1% of HPV-positive patients responding well, with 28.5% showing recurrence or residual disease, and 2.4% developing metastasis. Among HPV-negative patients, only 25% showed a good response, with significantly worse outcomes ($p = 0.019$)[8]. Harima et al. similarly found shorter survival in HPV-negative cervical carcinoma patients compared to HPV-positive cases[10]. The differences in findings may stem from the small number of HPV-negative case in our study. Chun Chen et al. (2010) studied the clinical impact of HPV genotypes in 1,010 cervical cancer patients who underwent radiotherapy from 1993 to 2000[15]. Using a gene chip to detect 38 HPV types, they found that HPV-negative tumors were associated with poorer survival outcomes. The study established HPV genotype as a key prognostic factor for survival in cervical cancer patients receiving radiotherapy In studied population, HPV 16 was the most prevalent subtype among cervical cancer patients undergoing chemoradiotherapy, regardless of treatment response. Poor responses were observed in various HPV subtypes, including HPV 16, 18, 33, 56, and 58, while HPV 16 was still predominant in patients with a good response, suggesting its complex role. Overall, complete response rates ranged from 67.4% to 80.4%. In comparison, Gupta et al. found 78.6% of HPV 16-positive patients had a good response, while only 33.3% of HPV 18-positive patients responded favorably ($p = 0.023$)[8]. HPV 16-positive tumors showed a better treatment response than HPV 18-positive tumors. Our findings align with King et al., who founded no significant difference in recurrence between HPV 16 and HPV 18 positive patients[16]. Onuki et al. suggested that HPV 16 DNA detection might indicate a favorable prognosis in cervical cancer patients[9], whereas our study found no significant impact of HPV genotype on chemoradiotherapy response. This highlights the need for further research to explore underlying mechanisms and optimize treatment strategies. The limited number of HPV-negative cases in our study emphasizes the importance of broadening research with larger patient cohorts. Understanding the specific HPV subtype's effect on clinical characteristics, biological behavior, and

treatment response, along with exploring new biomarkers, could enhance prognostic accuracy and improve cervical cancer management.

5. CONCLUSION

The study underscores the significance of HPV status as a prognostic factor for chemoradiotherapy treatment response in cervical cancer. HPV-positive tumors showed significantly better outcomes, highlighting the value of HPV testing in guiding treatment decisions and prognosis assessment.Although some clinical trials have shown that HPV genotype can affect treatment outcomes in cervical cancer, our prospective study found no significant impact of HPV genotype on chemoradiotherapy response. The small sample size of HPV-negative cases emphasizes the need for further research with larger patient populations. Investigating the specific HPV sub type in cervical carcinoma could provide insights into clinical characteristics, biological behaviors, and treatment responses. The last response of treatment in different cases can also an area of research.The high prevalence of HPV16 among all the HPV positive studied population elaborates the benefit of new vaccines which are designed to target HPV 16 and 18. Future studies should focus on comprehensive reporting of clinical outcomes, treatment response rates, and the identification of new biomarkers to improve prognostic accuracy.

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