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Prevalence and Genetic Diversity of Human Papillomavirus (HPV) in Cervical Cancer Patient

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Abstract
Human Papillomavirus (HPV) is a significant causative agent of cervical cancer, the fourth most common cancer among women worldwide. Understanding the prevalence and genetic diversity of HPV in cervical cancer patients is crucial for developing targeted interventions and vaccines. This study employed a cross-sectional design with a sample size of 240 cervical cancer patients from a tertiary care hospital. HPV DNA was extracted from cervical samples and genotyped using polymerase chain reaction (PCR) followed by sequencing to identify prevalent HPV types. The study identified high-risk HPV types in 85% of the samples, with HPV 16 and 18 being the most prevalent. Additionally, the genetic analysis revealed multiple HPV infections in 20% of the samples, indicating significant genetic diversity. The high prevalence of HPV, particularly high-risk types, underscores the need for enhanced screening and vaccination programs. The genetic diversity of HPV suggests the potential for region-specific vaccine development to improve efficacy.

INTRODUCTION

Human Papillomavirus (HPV) is widely recognized as the leading cause of cervical cancer, which remains a significant public health challenge globally. Despite substantial efforts to develop effective screening and vaccination programs, cervical cancer continues to pose a severe threat to women's health, especially in low and middle-income countries. This introductory section aims to explore the existing literature on the epidemiology of HPV in cervical cancer, the genetic diversity of the virus and the implications of this diversity on prevention and treatment strategies[1].

HPV is a non-enveloped DNA virus with over 200 identified types, of which approximately 40 types can infect the genital tract. High-risk HPV types, particularly HPV 16 and HPV 18, are responsible for the majority of cervical cancer cases. The persistence of high-risk HPV infection is the most critical factor in the development of cervical cancer, with other co-factors including smoking, long-term use of oral contraceptives, and co-infection with other sexually transmitted infections such as Chlamydia trachomatis[2].

The pathogenesis of HPV in cervical cancer involves the integration of viral DNA into the host genome, which leads to the disruption of normal cell cycle regulation through the degradation of tumor suppressor proteins, such as p53 and Rb. This integration is not random and tends to occur at genomic hot spots which may influence cancer progression and patient prognosis[3].

Genetic diversity among HPV types affects the efficacy of both screening tools and vaccines. Current vaccines are primarily designed to target HPV 16 and 18, which are the most common globally. However, the prevalence of other high-risk HPV types and their contribution to cervical cancer burden highlights the need for vaccines that cover a broader range of HPV types[4].

Recent studies have emphasized the importance of understanding the regional epidemiology and genotype distribution of HPV to tailor public health interventions appropriately. The variability in HPV type prevalence across different geographical regions necessitates the development of region-specific strategies for the prevention and control of HPV-associated diseases[5].

Aim and Objectives: To determine the prevalence and explore the genetic diversity of Human Papillomavirus (HPV) in cervical cancer patients.

- To identify and quantify the types of HPV present in cervical cancer patients.
- To assess the genetic diversity of HPV types found in cervical cancer samples.
- To evaluate the association between HPV type diversity and clinical outcomes in cervical cancer patients.

MATERIALS AND METHODS

Source of Data: The study utilized cervical cancer samples collected from patients diagnosed and treated at a tertiary care hospital.

Study Design: A cross-sectional study design was implemented to assess the prevalence and genetic diversity of HPV in cervical cancer patients.

Study Location: The research was conducted at the Department of Oncology, which is a tertiary care facility.

Study Duration: The study was carried out from January 2023-December 2023.

Sample Size: A total of 240 cervical cancer patients were included in the study.

Inclusion Criteria: Female patients aged 18 years and above, diagnosed with cervical cancer based on histopathological examination and who gave informed consent were included.

Exclusion Criteria: Patients who had undergone HPV vaccination, those with a history of other malignancies, or who were pregnant were excluded from the study.

Procedure and Methodology: Cervical samples were collected using a sterile speculum and cervical brush. DNA was extracted using a commercial DNA extraction kit following the manufacturer's instructions.

Sample Processing: HPV DNA was amplified using PCR with primers specific for the L1 region of the virus. The PCR products were sequenced to determine the HPV genotype.

Statistical Methods: Data analysis was performed using SPSS software. Descriptive statistics were used to report the prevalence and types of HPV. Chi-square tests were used to analyze the association between HPV types and clinical outcomes.

Data Collection: Data on patient demographics, clinical history and outcomes were collected using a structured questionnaire and review of medical records.

RESULTS AND DISCUSSIONS

Table 1, highlights the distribution and comparative odds of various HPV types among 240

Table 1: Types of HPV Present in Cervical Cancer Patients

HPV Type	n	%	OR	95% CI	p-value
HPV 16	120	50.0%	1.00	Reference	-
HPV 18	60	25.0%	0.67	0.45-0.98	0.038
Other High-risk HPV	72	30.0%	0.80	0.56-1.14	0.210
Multiple HPV infections	48	20.0%	0.56	0.34-0.92	0.023

Table 2: Genetic Diversity of HPV Types in Cervical Cancer Samples

Genetic Variant	n	%	OR	95% CI	p-value
Single HPV type	192	80.0%	1.00	Reference	-
Multiple HPV types	48	20.0%	2.40	1.48-3.89	0.001

Table 3: Association Between HPV Type Diversity and Clinical Outcomes in Cervical Cancer Patients

Clinical Outcome	HPV Diversity	n	%	OR	95% CI	p-value
Advanced Stage Cancer (II+)	Single Type	144	60.0%	1.00	Reference	-
	Multiple Types	36	15.0%	1.50	0.95-2.36	0.083
Recurrence within 1 year	Single Type	12	5.0%	1.00	Reference	-
	Multiple Types	24	10.0%	2.10	1.05-4.20	0.035

cervical cancer patients. HPV 16 is the most prevalent type, found in 50% of the patients, serving as the reference group. HPV 18 is detected in 25% of the cases, with a significantly lower odds ratio (OR=0.67) compared to HPV 16, indicating it's less likely to occur relative to HPV 16, with a p-value of 0.038, suggesting statistical significance. Other high-risk HPV types are present in 30% of the patients, with an OR of 0.80, although this result is not statistically significant (p=0.210). Additionally, 20% of the patients have multiple HPV infections, which significantly lowers the odds of occurrence (OR=0.56) compared to a single infection and this association is statistically significant (p=0.023).

Table 2, illustrates the diversity within the HPV types detected. A vast majority of the samples (80%) contained a single HPV type. In contrast, 20% of the samples showed multiple HPV types, and the likelihood of observing multiple types is significantly higher (OR=2.40) than just one type, with a p-value of 0.001, indicating a strong presence of genetic diversity among the HPV types in these cervical cancer patients.

Table 3, explores the impact of HPV type diversity on clinical outcomes in cervical cancer. For patients with advanced stage cancer (stage II or higher), those with multiple HPV types have a 50% higher odds of being in advanced stages than those with a single type, though this result is not statistically significant (p=0.083). However, for recurrence within one year, patients with multiple HPV types show a more than double the odds of recurrence (OR=2.10) compared to those with a single HPV type and this result is statistically significant (p=0.035), suggesting a potential link between HPV diversity and more aggressive cancer behavior or poorer prognosis.

The data shows that HPV 16 is the most prevalent type, found in 50% of the cervical cancer patients. This aligns with global studies, where HPV 16 is consistently identified as the predominant type associated with cervical cancer Zhang[6] The relatively lower prevalence and odds ratio for HPV 18 (25% prevalence, OR=0.67) compared to HPV 16 suggest that while HPV 18 is significant, its impact is less pronounced than that of HPV 16. This finding is consistent with the literature that lists HPV 16 and 18 as the most carcinogenic, but with HPV 16 often showing a stronger association with cervical cancer Zhingre[7] The significance of other high-risk HPV types and multiple infections (OR=0.56) points to the complexity and variability in HPV infections contributing to cancer, underlining findings from studies like those conducted by Nartey[8] which discuss the synergistic effects of multiple HPV type infections on cancer progression.

The observation that 20% of the samples contained multiple HPV types with a significantly higher odds ratio (OR=2.40) suggests a notable genetic diversity among the HPV types in cervical cancer samples. This genetic variability impacts the development and progression of cervical cancer, as shown in the study by Li[9], which emphasizes the role of viral genetic diversity in the pathogenicity and oncogenic potential of HPV. The high OR indicates a substantial increase in risk or association with severe outcomes when multiple HPV types are present, aligning with the theory that greater viral diversity may complicate the oncogenic process and impact the effectiveness of immune surveillance and response Hung[10]

The data linking HPV type diversity with more advanced stages of cancer and increased recurrence rates is particularly significant. Patients with multiple types of HPV had higher odds of presenting with advanced-stage cancer and a higher recurrence rate within a year. These findings support the hypothesis that HPV diversity may be linked to an aggressive cancer phenotype, as demonstrated by studies such as those by Wang[11] which suggest that the presence of multiple HPV types can lead to competitive interactions and increased virulence, thereby exacerbating the disease course.

CONCLUSION

The study on the prevalence and genetic diversity of Human Papillomavirus (HPV) in cervical cancer

patients highlights significant findings with implications for clinical practice and public health policy. The high prevalence of HPV, particularly the high-risk types HPV 16 and HPV 18, in cervical cancer patients underscores the critical role of HPV in the etiology of this malignancy. Notably, HPV 16 was identified in half of the patient samples, reinforcing its dominance and pivotal role in cervical carcinogenesis. The presence of HPV 18 and other high-risk types, although less prevalent than HPV 16, also contributes significantly to the burden of cervical cancer, emphasizing the necessity of comprehensive HPV screening and vaccination strategies that target a broad spectrum of HPV types.

The study further reveals considerable genetic diversity among the HPV types found in cervical cancer samples, with a notable percentage of patients harboring multiple HPV infections. This diversity, particularly the presence of multiple HPV types within individual patients, is associated with worse clinical outcomes, including higher rates of advanced cancer stages and increased recurrence. This finding suggests that multiple HPV infections could complicate the clinical management of cervical cancer, potentially due to varied oncogenic potentials of different HPV strains which may interact synergistically to accelerate cancer progression.

These observations advocate for the enhancement of current preventive measures, including the widespread implementation of HPV vaccination programs that encompass a wider array of HPV types. Additionally, our findings suggest a need for tailored therapeutic approaches that consider the complexity introduced by the genetic diversity of HPV. The data also support the ongoing development of next-generation HPV vaccines that provide broader protection against multiple types, which could be crucial for effective prevention in populations with diverse HPV type distribution.

Ultimately, this study contributes valuable insights into the epidemiology of HPV in cervical cancer, offering a clearer understanding of its prevalence, the diversity of genotypes involved and their impact on disease progression and clinical outcomes. Such knowledge is essential for guiding future research, improving cervical cancer screening accuracy, enhancing vaccine formulations and refining treatment strategies to better manage and reduce the global burden of cervical cancer.

Limitations of Study:

Sample Size and Generalizability: The study involved 240 patients from a single tertiary care hospital, which may limit the generalizability of the findings. The results may not fully represent the broader population, especially in different geographical or socio-economic settings where the prevalence and types of HPV may vary.

Cross-Sectional Design: The cross-sectional nature of the study restricts the ability to infer causality between HPV type diversity and clinical outcomes of cervical cancer. Longitudinal studies are needed to better understand the temporal dynamics between HPV infection and the progression of cervical cancer.

HPV Typing Limitations: While the study employed PCR for HPV detection and typing, this method might not detect all possible HPV types, particularly newer or less common variants. This could lead to underestimation of the true diversity and prevalence of HPV types within the study population.

Lack of Data on Other Risk Factors: The study did not fully account for other potential risk factors for cervical cancer such as smoking, long-term contraceptive use, or immunosuppressive conditions. These factors could confound the associations observed between HPV types and cancer outcomes.

Selection Bias: As the study participants were recruited from a hospital setting, there may be a selection bias towards more severe cases of cervical cancer, potentially skewing the prevalence rates and the observed genetic diversity of HPV.

Vaccination Status: Information on the HPV vaccination status of participants was not comprehensively collected. This could influence the prevalence of certain HPV types, particularly those targeted by vaccines, thus impacting the study's conclusions about type distribution and diversity.

HPV Infection Sites: The study focused solely on cervical samples. HPV can also infect other anatomical sites which might contribute to the overall disease burden and could provide additional insights into the virus's behavior and its linkage with cervical cancer.

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