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Research Article

Prevalence of HPV in Oral Squamous Cell Carcinoma Patients

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ABSTRACT

Background: Human Papillomavirus (HPV) has been established as a contributing factor in various cancers, with increasing evidence linking it to Oral Squamous Cell Carcinoma (OSCC). This study aims to determine the prevalence of HPV in OSCC patients and identify the most frequent HPV types associated with the disease. **Methods:** A cross-sectional study was conducted on 200 patients diagnosed with OSCC at a tertiary care center. Samples were collected and tested for HPV DNA using Polymerase Chain Reaction (PCR) targeting high-risk HPV types. Demographic and clinical data were also analyzed to assess correlations between HPV status and clinical characteristics such as age, sex, and tumor stage. **Results:** Out of the 200 patients, 32% tested positive for HPV. HPV-16 was the most prevalent type, found in 24% of the patients, followed by HPV-18, HPV-31, and other types at lower frequencies. Statistical analysis revealed significant associations between HPV positivity and younger age (<40 years), male sex, and advanced tumor stages (III-IV). **Conclusion:** The study confirms a significant presence of HPV in patients with OSCC, predominantly HPV-16. The high prevalence in younger patients and those with advanced disease stages suggests that HPV is an important factor in the etiology and progression of OSCC. These findings highlight the need for further research into HPV as a marker for early detection and a potential target for vaccination and therapeutic strategies in OSCC.

Keywords: Human Papillomavirus, Oral Squamous Cell Carcinoma, Hpv Prevalence.

INTRODUCTION

Oral Squamous Cell Carcinoma (OSCC) represents a significant portion of head and neck cancers, characterized by aggressive growth and substantial morbidity. Recent advancements in molecular biology and epidemiology have pointed to the Human Papillomavirus (HPV) as a potential etiological factor in OSCC, alongside traditional risk factors such as tobacco use and alcohol consumption. The association between HPV and OSCC prompts a re-evaluation of preventive strategies, diagnostic methods, and therapeutic approaches.[1][2]

The discovery of high-risk HPV types, particularly HPV-16 and HPV-18, in oropharyngeal cancers has led to a paradigm shift in understanding the pathogenesis of these malignancies. Unlike other head and neck cancers, HPV-positive OSCC tends to affect a younger demographic and carries a different prognosis and clinical outcome. This recognition has heightened interest in studying the prevalence of HPV in OSCC populations to better characterize its epidemiology, clinical features, and outcomes.[3][4]

The prevalence of HPV in OSCC varies globally, reflecting differences in social behaviors, genetic predispositions, and environmental exposures. Studies have shown varying prevalence rates across different geographical and demographic groups, suggesting that HPV's role in OSCC may be influenced by regional and lifestyle factors. Moreover, the mechanism by which HPV contributes to carcinogenesis in the oral cavity is not fully understood, although it is believed to involve viral integration and the disruption of cell cycle regulation by viral oncoproteins, such as E6 and E7.[5]

Early detection of HPV in OSCC can significantly affect management strategies, impacting decisions regarding prognosis, treatment options, and follow-up protocols. Thus, understanding the epidemiological link between HPV and OSCC is crucial for developing targeted interventions and improving patient outcomes. Additionally, the potential for HPV vaccines in preventing HPV-associated OSCC presents a promising avenue for reducing the burden of this cancer.[6]

Aim

To determine the prevalence of Human Papillomavirus (HPV) in patients diagnosed with Oral Squamous Cell Carcinoma.

Objectives

1. To identify the types of HPV most frequently associated with OSCC in the studied population.
2. To assess the correlation between HPV status and various clinical parameters such as age, sex, and tumor stage in OSCC patients.

MATERIAL AND METHODOLOGY

Source of Data

The data for this study were collected from patients diagnosed with Oral Squamous Cell Carcinoma at a major oncology center.

Study Design

This was a cross-sectional study designed to investigate the prevalence of HPV in OSCC patients.

Study Location

The study was conducted at the Comprehensive Cancer Center, which serves as a referral center for head and neck cancers.

Study Duration

The research spanned from January 2022 to December 2023.

Sample Size

A total of 200 patients diagnosed with OSCC were included in the study.

Inclusion Criteria

Included were patients diagnosed with OSCC based on histopathological examination, regardless of their age, sex, and cancer stage.

Exclusion Criteria

Patients with a history of any other malignancies, previous head and neck cancers, or those who had undergone chemotherapy or radiation therapy for any cancer before the diagnosis of OSCC were excluded.

Procedure and Methodology

All selected patients underwent a detailed clinical evaluation followed by the collection of tissue samples during biopsies or surgical resections.

Sample Processing

The collected samples were processed to extract DNA, which was then tested for HPV DNA by Polymerase Chain Reaction (PCR) using primers specific for high-risk HPV types.

Statistical Methods

Data were analyzed using SPSS software. The prevalence of HPV was calculated and correlations with clinical parameters were assessed using chi-square tests and logistic regression.

Data Collection

Data were collected through patient medical records, interviews, and direct clinical assessments to obtain comprehensive demographic and clinical information.

OBSERVATION AND RESULTS

Table 1: Types of HPV Most Frequently Associated With OSCC

HPV Type	Patients Tested (n=200)	HPV Positive (n, %)	95% CI	P-value
HPV-16	200	48 (24%)	18.1% - 29.9%	<0.001
HPV-18	200	12 (6%)	3.1% - 8.9%	0.010
HPV-31	200	8 (4%)	1.7% - 6.3%	0.022
HPV-33	200	5 (2.5%)	0.8% - 4.2%	0.110
Others	200	11 (5.5%)	2.8% - 8.2%	0.050

Table 1 presents the prevalence of various HPV types among 200 patients tested for their association with Oral Squamous Cell Carcinoma (OSCC). HPV-16 emerged as the most frequently detected type, found in 48 patients, accounting for 24% of the sample,

which significantly confirms its strong association with OSCC (P < 0.001). The confidence interval (CI) for this type ranged from 18.1% to 29.9%. HPV-18 and HPV-31 were also present but with lower prevalence rates of 6% and 4%, respectively, also showing significant associations with P-values of 0.010 and 0.022. HPV-33 was found in 2.5% of the patients, but its association was not statistically significant (P = 0.110), suggesting a less definitive link with OSCC. The category labeled "Others" encompassed a variety of less common HPV types, collectively found in 5.5% of the patients, also with a significant P-value of 0.050.

Table 2: Correlation between HPV Status and Clinical Parameters in OSCC Patients

Clinical Parameter	Category	HPV Positive (n, %)	95% CI	P-value
Age Group				
- <40 years	40 (20%)	20 (50%)	34.9% - 65.1%	0.003
- 40-60 years	100 (50%)	32 (32%)	23.0% - 41.0%	0.045
- >60 years	60 (30%)	12 (20%)	10.4% - 29.6%	0.200
Sex				
- Male	130 (65%)	45 (34.6%)	26.4% - 42.8%	0.040
- Female	70 (35%)	19 (27.1%)	17.2% - 37.0%	0.122
Tumor Stage				
- Stage I-II	120 (60%)	30 (25%)	17.6% - 32.4%	0.038
- Stage III-IV	80 (40%)	34 (42.5%)	32.0% - 53.0%	0.004

Table 2 explores the correlation between HPV positivity and various clinical parameters in OSCC patients. Starting with age, patients under 40 years showed a remarkably high prevalence of HPV positivity (50%) with a significant association (P = 0.003). In the 40-60 years age group, 32% were HPV positive, also showing a significant association (P = 0.045). The prevalence of HPV positivity declines to 20% in patients over 60 years, with no significant association (P = 0.200), suggesting a stronger HPV linkage in younger patients. Regarding sex, 34.6% of males were HPV positive compared to 27.1% of females; however, the association was only significant in males (P = 0.040). In terms of tumor stage, patients with more advanced disease (Stage III-IV) exhibited a higher rate of HPV positivity (42.5%) compared to those with Stage I-II (25%), with both categories showing significant associations (P = 0.038 for Stage I-II and P = 0.004 for Stage III-IV), indicating a potential role of HPV in more aggressive disease forms.

DISCUSSION

Table 1: Types of HPV Most Frequently Associated with OSCC

The findings from Table 1 highlight HPV-16 as the predominant type found in Oral Squamous Cell Carcinoma (OSCC) patients, with a prevalence of 24%. This is consistent with other studies which have also identified HPV-16 as the most significant HPV type associated with head and neck cancers, particularly OSCC. A study by D'Souza G et al.(2017)[7] noted similar prevalence rates and emphasized the oncogenic potential of HPV-16 in the oral epithelium. The significantly lower prevalence of other HPV types such as HPV-18, HPV-31, and HPV-33 suggests that while these types contribute to OSCC, their role is less dominant compared to HPV-16.

HPV-18, which was found in 6% of the cases, aligns with data from Oliveira AC et al.(2022)[8], who reported slightly lower prevalence rates in a similar population. The presence of HPV-31 and HPV-33 in smaller percentages further supports the notion that multiple high-risk HPV types, albeit to a varying degree, are involved in OSCC pathogenesis.

The statistical significance of these findings, especially the high p-values for less common types like HPV-33, indicates the need for more targeted HPV typing in OSCC patients, as also suggested by other research findings which highlight the variability in HPV type prevalence across different geographic and demographic groups Purwanto DJ et al.(2020)[9] & de Abreu PM et al.(2018)[10]

The results from Table 2 indicate significant correlations between HPV positivity and various clinical parameters such as age, sex, and tumor stage. The highest HPV prevalence in patients under 40 years (50%) could reflect behavioral patterns such as early sexual activity, aligning with studies like Dalakoti P et al.(2019)[11], which noted the impact of early sexual behaviors on HPV-related OSCC risk.

The decline in prevalence with age, shown in this study, could indicate an immune clearance over time, or less exposure to risk factors in older populations. Gillison ML et al.(2015)[12]
The male predominance (34.6%) in HPV-positive OSCC cases corresponds with broader epidemiological data, which often shows a higher incidence of HPV-associated head and neck cancers among males, potentially due to differences in lifestyle or hormonal factors that could influence HPV persistence Lima MA et al.(2014)[13] & Chi AC et al.(2015)[14].
The significant association between advanced tumor stages (Stage III-IV) and higher HPV positivity (42.5%) provides crucial insights into the aggressive nature of HPV-driven OSCC, consistent with findings from Polz-Gruszka D et al.(2015)[15] & Kansy K et al.(2014)[16] that showed improved survival rates but more aggressive tumor characteristics in HPV-positive cases.

CONCLUSION

The study on the prevalence of Human Papillomavirus (HPV) in patients with Oral Squamous Cell Carcinoma (OSCC) has provided significant insights into the epidemiological and clinical aspects of HPV in relation to OSCC. The findings reveal that HPV, particularly HPV-16, is a prevalent infectious agent in OSCC patients, with a marked presence noted in 24% of the cases studied. This emphasizes HPV-16's dominant role in the etiology of these cancers, which aligns with global research that identifies high-risk HPV types as critical factors in the pathogenesis of not only cervical but also oropharyngeal and oral cancers.
The study further illustrated how HPV prevalence varies significantly with clinical parameters such as age, gender, and tumor stage. Notably, younger patients under 40 years displayed a higher rate of HPV positivity, suggesting that HPV-related OSCC may affect younger populations prominently, likely due to behavioral factors such as early onset of sexual activity and higher numbers of sexual partners. Moreover, males were more frequently affected by HPV-positive OSCC than females, and advanced tumor stages were more commonly associated with HPV positivity, highlighting the aggressive nature of HPV-associated OSCC.
These findings underscore the necessity for heightened awareness and targeted screening for HPV in populations at risk for OSCC. Additionally, they support the potential for HPV vaccination as a preventive measure, which could significantly impact the incidence of OSCC among younger demographics. Implementing robust HPV screening and vaccination protocols could therefore serve as crucial strategies in reducing the burden of OSCC, improving early detection, and enhancing patient outcomes through more tailored and effective treatment strategies.
In conclusion, this study not only confirms the significant role of HPV in OSCC but also highlights the need for comprehensive strategies that incorporate HPV vaccination, screening, and public health initiatives to mitigate the impact of this virus on oral cancer prevalence and patient health globally.

Limitations of Study

1. Cross-Sectional Design

The cross-sectional nature of the study limits the ability to establish causality between HPV infection and the development of OSCC. Longitudinal studies would be more informative in understanding the temporal relationship and the progression from HPV infection to cancer development.

2. Single-Center Data Collection

Data were collected from a single cancer center, which might not represent the broader OSCC patient population. Multi-center studies could provide a more comprehensive understanding of HPV prevalence across different geographic and demographic groups, enhancing the generalizability of the findings.

3. HPV Typing Limitations

The study primarily focused on the most common high-risk HPV types but did not extensively cover all HPV types known to be associated with OSCC. This could underestimate the true prevalence of HPV in the OSCC population, as less common or emerging HPV types might also play a role in the pathogenesis of these cancers.

4. Lack of Behavioral Data

The study did not collect comprehensive data on risk factors such as sexual behavior, smoking, and alcohol consumption, which are critical in understanding the modes of HPV transmission and its role in OSCC. Inclusion of these factors could enhance the understanding of the interplay between lifestyle risks and HPV status.

5. Variability in Diagnostic Techniques

The study used Polymerase Chain Reaction (PCR) for detecting HPV DNA, which is highly sensitive but does not distinguish between transient infections and those that are biologically significant to cancer development. The use of additional diagnostic methods, such as p16 immunohistochemistry, could provide a more accurate assessment of the oncogenic potential of the detected HPV.

6. Sample Size and Power

Although the sample size of 200 may be adequate for detecting prevalence, it may not be sufficient to perform sub-group analyses or to detect differences among less common HPV types or less frequent clinical outcomes. A larger sample size would improve the statistical power of the study and allow for more detailed analyses.

7. Potential Selection Bias

The study population may include a disproportionate number of advanced cases or patients who have other co-morbidities, which could influence the prevalence rates and the generalizability of the findings to all OSCC patients.

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