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Original Research

To evaluate the prevalence of HPV in different oral lesions, including both benign and malignant conditions

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ABSTRACT:
Aim: To evaluate the prevalence of HPV in different oral lesions, including both benign and malignant conditions. **Material and Methods:** The study was conducted in the Department of Oral and Maxillofacial Pathology at a tertiary care hospital.The study included a total of 100 patients who presented with oral lesions. A detailed clinical examination of the oral cavity was performed by an experienced oral medicine specialist to identify and document the type, location, and characteristics of the oral lesions. This examination was crucial for accurately classifying the lesions and guiding subsequent sample collection.Histopathological examination of the tissue samples was performed by a pathologist to confirm the diagnosis of the lesions as either benign or malignant. **Results:** Among the 100 oral lesion cases, HPV positivity varied based on the lesion type. In benign lesions, 28.6% of leukoplakia cases tested positive for HPV, while 20% of oral lichen planus cases were HPV positive. In contrast, HPV prevalence was significantly higher in malignant lesions, with 45% of oral squamous cell carcinoma cases testing positive for HPV. This suggests a stronger association between HPV and malignant lesions, particularly oral squamous cell carcinoma, compared to benign conditions.The histopathological analysis confirmed that malignant lesions had a higher prevalence of HPV. Of the 60 benign lesions, 15 tested positive for HPV, representing 25% of the benign cases. In contrast, 18 out of 40 malignant lesions were HPV positive, yielding a prevalence of 45%. Overall, 33% of the total 100 oral lesions tested positive for HPV. The higher prevalence of HPV in malignant lesions suggests that HPV may play a more significant role in the pathogenesis of oral cancers compared to benign conditions. **Conclusion:** We concluded that the HPV prevalence was higher in malignant oral lesions, particularly oral squamous cell carcinoma, compared to benign lesions. Clinical presentations such as ulcers and red patches, as well as lesions located on the tongue and palate, were more likely to be associated with HPV infection. Larger lesions also showed a greater likelihood of HPV positivity. These results highlight the potential role of HPV in the development of malignant oral lesions and suggest the importance of considering HPV testing in patients with specific lesion characteristics.
Keywords: HPV, Oral lesions, Benign, Malignant

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INTRODUCTION

Human Papillomavirus (HPV) is a small, non-enveloped DNA virus that has garnered significant attention in medical research due to its association with a wide range of epithelial lesions, including those found in the oral cavity. HPV is well-known for its role in the pathogenesis of cervical cancer, but its involvement in oral lesions, both benign and malignant, has become an area of growing interest and concern.[1]HPV is primarily transmitted through direct contact with infected skin or mucous membranes. In the context of oral lesions, the transmission of HPV can occur through oral-genital contact, direct mouth-to-mouth contact, or even indirectly through fomites. The virus infects the basal cells of the epithelium, where it can remain latent or integrate into the host genome, leading to cellular changes that may progress to malignancy over time.[2]The oral cavity is a complex environment, hosting a variety of tissues that can be affected by HPV. These include the lips, tongue, floor of the mouth, palate, gingiva, and buccal mucosa. The types of lesions that can develop in these areas range

from benign conditions, such as oral papillomas and leukoplakia, to potentially malignant disorders like oral lichen planus, and overtly malignant cancers, most notably oral squamous cell carcinoma (OSCC). The variability in the clinical presentation of HPV-related oral lesions adds to the complexity of diagnosis and treatment.[3]Benign oral lesions associated with HPV include verrucous lesions, such as squamous papilloma, verruca vulgaris, and condyloma acuminatum. These lesions are generally non-cancerous but can cause discomfort and aesthetic concerns for patients. Squamous papilloma, for instance, is the most common benign epithelial neoplasm of the oral cavity and is typically caused by low-risk HPV types, such as HPV-6 and HPV-11. These lesions appear as small, cauliflower-like growths that are often found on the tongue, lips, and buccal mucosa. While they are benign, there is always a concern about potential malignant transformation, especially in immunocompromised individuals.[4]

Leukoplakia, another benign condition, is characterized by white patches on the oral mucosa that cannot be wiped off. It is considered a potentially malignant disorder because a proportion of these lesions may eventually progress to cancer, particularly when associated with high-risk HPV types like HPV-16 and HPV-18. The role of HPV in the malignant transformation of leukoplakia is still under investigation, but it is believed that HPV infection may contribute to the disruption of cellular regulatory mechanisms, leading to dysplasia and, ultimately, carcinoma.[5]Oral lichen planus is another chronic inflammatory condition that affects the mucous membranes of the mouth. It presents as white, lacy patches, sometimes accompanied by painful sores. The exact etiology of oral lichen planus is unknown, but it is thought to be an autoimmune disorder with a possible link to HPV in certain cases. Although the direct association between HPV and oral lichen planus is less clear than with other lesions, studies have suggested that HPV might play a role in the pathogenesis of a subset of these cases, particularly those that exhibit dysplastic features.[6]The most concerning HPV-related oral condition is oral squamous cell carcinoma (OSCC), a malignant tumor that arises from the squamous cells lining the oral cavity. OSCC is the most common type of oral cancer and is often associated with high-risk HPV types, particularly HPV-16. The involvement of HPV in OSCC has shifted the paradigm of oral cancer etiology, which was traditionally linked to tobacco and alcohol use. HPV-positive OSCC tends to occur in younger patients and is often located in the oropharynx, particularly in the tonsils and base of the tongue. These cancers are biologically distinct from their HPV-negative counterparts, often presenting with different molecular profiles, better responses to treatment, and overall improved prognoses.[7]The molecular mechanisms by which HPV contributes to the development of OSCC involve the expression of viral oncoproteins E6 and E7, which interfere with the tumor suppressor functions of p53 and retinoblastoma (Rb) proteins, respectively. This disruption leads to uncontrolled cell proliferation, genomic instability, and, eventually, malignant transformation. The recognition of HPV as a key factor in OSCC has important implications for prevention, diagnosis, and treatment. For instance, HPV vaccination, which has been highly effective in preventing cervical cancer, may also reduce the incidence of HPV-related oral cancers, although this potential benefit is still being studied.[8]In addition to the direct carcinogenic effects of HPV, the virus's presence in oral lesions may also complicate clinical management. HPV-positive lesions can be more challenging to treat due to their tendency to recur and their association with multifocal disease. Moreover, the presence of HPV in benign lesions raises questions about the necessity of more aggressive treatment approaches, such as surgical excision, to prevent potential malignant transformation.[9]The diagnosis of HPV-related oral lesions involves a combination of clinical examination, histopathological analysis, and molecular testing for HPV DNA. The identification of HPV in oral lesions can provide valuable prognostic information, particularly in the context of malignant conditions like OSCC. However, the clinical significance of HPV in benign lesions remains a topic of ongoing research, as the natural history of these infections and their potential for malignant transformation is not fully understood.[10]

MATERIAL AND METHODS

The study was conducted in the Department of Oral and Maxillofacial Pathology at a tertiary care hospital over a period of 12 months.The study included a total of 100 patients who presented with oral lesions. These patients were recruited from the outpatient department (OPD) of the hospital.Ethical approval was obtained from the Institutional Ethics Committee. Informed consent was obtained from all participants before their enrollment in the study.

Inclusion Criteria

Patients aged 18 years and above.

Patients presenting with clinically diagnosed oral lesions, including both benign (e.g., leukoplakia, oral lichen planus) and malignant conditions (e.g., oral squamous cell carcinoma).

Patients who consented to participate in the study.

Exclusion Criteria

- Patients with a history of HPV vaccination.
- Patients with a history of treatment for oral cancer (e.g., chemotherapy, radiotherapy).
- Patients with systemic conditions that could affect oral lesions (e.g., immunocompromised states).
- Patients who did not consent to participate in the study.

Methodology

A detailed clinical examination of the oral cavity was performed by an experienced oral medicine specialist to identify and document the type, location, and characteristics of the oral lesions. This examination was crucial for accurately classifying the lesions and guiding subsequent sample collection.

For sample collection, a biopsy was performed on the identified lesions under local anesthesia. Tissue samples were collected from both benign and malignant lesions. In cases where a biopsy was not feasible, a brush biopsy was performed to collect cells from the lesion surface. This method ensured that sufficient material was obtained for HPV detection and histopathological analysis.

The collected tissue samples were preserved in appropriate media and sent to the pathology laboratory for histopathological examination and HPV DNA detection. HPV DNA detection was carried out using polymerase chain reaction (PCR) techniques to identify the presence of HPV types known to be associated with oral lesions. This molecular approach provided high sensitivity and specificity in detecting HPV.

Histopathological examination of the tissue samples was performed by a pathologist to confirm the diagnosis of the lesions as either benign or malignant. The histopathological findings were then correlated with the HPV detection results, allowing for an integrated analysis of the relationship between HPV presence and the nature of the oral lesions.

The primary outcome measure of the study was the prevalence of HPV in the oral lesions examined. Secondary outcomes included the correlation between HPV presence and the type of lesion (benign vs. malignant) and the specific characteristics of the lesions, providing insight into the potential role of HPV in the pathogenesis of these conditions.

Data Analysis

For data analysis SPSS version 25.0 were used. Descriptive statistics were used to summarize the prevalence of HPV in the different types of oral lesions. The prevalence of HPV in benign lesions was compared to that in malignant lesions using appropriate statistical tests, such as the chi-square test. Additionally, the association between HPV presence and lesion characteristics (e.g., size, location) was analyzed to explore potential patterns and risk factors.

RESULTS

Demographic Characteristics of the Study Population (Table 1)

The study included 100 patients, with a nearly even distribution across age groups. The largest group was aged 40-49 years, comprising 30% of the sample, followed by the 30-39 and 50-and-above age groups (25% each). Patients aged 18-29 years accounted for 20% of the sample. There was a slight male predominance, with 55% of the patients being male and 45% female. The distribution of oral lesions revealed that 60% of the cases were benign, including conditions such as leukoplakia and oral lichen planus, while 40% of the cases were malignant, primarily oral squamous cell carcinoma.

Prevalence of HPV in Oral Lesions (Table 2)

Among the 100 oral lesion cases, HPV positivity varied based on the lesion type. In benign lesions, 28.6% of leukoplakia cases tested positive for HPV, while 20% of oral lichen planus cases were HPV positive. In contrast, HPV prevalence was significantly higher in malignant lesions, with 45% of oral squamous cell carcinoma cases testing positive for HPV. This suggests a stronger association between HPV and malignant lesions, particularly oral squamous cell carcinoma, compared to benign conditions.

Clinical Presentation of Oral Lesions in Relation to HPV Status (Table 3)

When analyzing HPV positivity in relation to the clinical presentation of the lesions, certain patterns emerged. Ulcers and red patches showed the highest HPV prevalence, each with 40% of cases testing positive for the virus. White patches had an HPV prevalence of 32%, while exophytic growths and verrucous lesions exhibited lower HPV positivity rates at 25% and 20%, respectively. This indicates that ulcers and red patches may have a higher likelihood of being associated with HPV infection compared to other types of lesions.

The location of the lesion also appeared to influence HPV prevalence. Lesions on the tongue and palate demonstrated the highest HPV positivity rates (40%), followed by the floor of the mouth (30%), gingiva (30%), and buccal mucosa (26.7%). These findings suggest that lesions located on the tongue and palate may have a higher association with HPV infection compared to those in other areas of the oral cavity.

Size of Lesion in Relation to HPV Status (Table 4)

The size of the lesions also showed a significant relationship with HPV positivity. Among lesions smaller than 1 cm, 10 cases tested positive for HPV, while 30 were negative, yielding a p-value of 0.032, indicating statistical significance. In lesions larger than 1 cm, 16 cases were HPV positive, and 22 were negative, with a p-value of 0.042, also suggesting significance. These findings indicate that larger lesions may be more likely to be associated with HPV infection, although smaller lesions also showed a notable HPV prevalence.

Histopathological Findings and HPV Detection (Table 5)

The histopathological analysis confirmed that malignant lesions had a higher prevalence of HPV. Of the 60 benign lesions, 15 tested positive for HPV, representing 25% of the benign cases. In contrast, 18

out of 40 malignant lesions were HPV positive, yielding a prevalence of 45%. Overall, 33% of the total 100 oral lesions tested positive for HPV. The higher prevalence of HPV in malignant lesions suggests that HPV may play a more significant role in the pathogenesis of oral cancers compared to benign conditions.

Table 1: Demographic Characteristics of the Study Population (N=100)

Characteristic	Number of Patients (n)	Percentage (%)
Age Group (years)		
18-29	20	20%
30-39	25	25%
40-49	30	30%
50 and above	25	25%
Gender		
Male	55	55%
Female	45	45%
Type of Oral Lesion		
Benign (e.g., leukoplakia, oral lichen planus)	60	60%
Malignant (e.g., oral squamous cell carcinoma)	40	40%

Table 2: Prevalence of HPV in Oral Lesions

Type of Lesion	Number of Cases (n)	HPV Positive (n)	HPV Prevalence (%)
Benign Lesions			
Leukoplakia	35	10	28.6%
Oral Lichen Planus	25	5	20.0%
Malignant Lesions			
Oral Squamous Cell Carcinoma	40	18	45.0%

Table 3. Clinical Presentation of Oral Lesions in Relation to HPV Status (N=100)

Clinical Presentation	Number of Cases (n)	HPV Positive (n)	HPV Negative (n)	HPV Prevalence (%)
Lesion Type				
Ulcer	30	12	18	40.0%
White Patch	25	8	17	32.0%
Red Patch	15	6	9	40.0%
Exophytic Growth	20	5	15	25.0%
Verrucous Lesion	10	2	8	20.0%
Location				
Tongue	30	12	18	40.0%
Buccal Mucosa	30	8	22	26.7%
Floor of Mouth	20	6	14	30.0%
Gingiva	10	3	7	30.0%
Palate	10	4	6	40.0%

Table 4: Size of Lesion

Size of Lesion	HPV Positive (n)	HPV Negative (n)	p-value
<1 cm	10	30	0.032
>1 cm	16	22	0.042

Table 5: Histopathological Findings and HPV Detection

Histopathological Diagnosis	Number of Cases (n)	HPV Positive (n)	HPV Prevalence (%)
Benign	60	15	25.0%
Malignant	40	18	45.0%
Total	100	33	33.0%

DISCUSSION

The demographic distribution of the study population, with the highest proportion of patients aged 40-49 years (30%), aligns with existing literature, which suggests that the prevalence of oral lesions increases with age. Similar age distributions were reported in studies by Dalla Torre et al. (2016) and Sudbø et al. (2004), where middle-aged and older adults were

more frequently diagnosed with oral lesions, particularly malignant ones.[11,12] The slight male predominance (55% male, 45% female) observed in our study is consistent with findings from other research, such as a study by Gillison et al. (2012), which reported a higher incidence of HPV-related oral lesions in males, potentially due to differences in risk factors such as smoking, alcohol consumption, and sexual behavior.[13]The higher proportion of benign lesions (60%) compared to malignant ones (40%) could reflect the general population's oral health status, where benign conditions like leukoplakia and oral lichen planus are more common. These findings are comparable to those of Holmstrup et al. (1988), who noted a higher prevalence of benign oral lesions in routine dental examinations, though the potential for malignant transformation, especially in leukoplakia, necessitates vigilance.[14]

The overall HPV positivity in our study was higher in malignant lesions (45%) compared to benign ones (28.6% for leukoplakia and 20% for oral lichen planus). These findings are in line with studies by Syrjänen et al. (1983) and Gillison et al. (2000), who both reported a significant association between HPV and oral squamous cell carcinoma, suggesting that HPV could be an important etiological factor in the development of these cancers.[15,16] In benign lesions, the lower prevalence of HPV might indicate that while HPV can be present, it plays a less central role in the pathogenesis of these conditions.The higher HPV prevalence in ulcers (40%) and red patches (40%) observed in our study corresponds with findings from Chen et al. (2017), who noted a higher HPV presence in more clinically aggressive and suspicious lesions, such as erythroplakia and ulcerative lesions . White patches, typically associated with conditions like leukoplakia, showed an HPV prevalence of 32%, which aligns with research indicating that a subset of leukoplakias, particularly those with dysplasia, may harbor HPV.[17]Regarding lesion location, our study found the highest HPV positivity in lesions on the tongue and palate (both 40%), which mirrors findings by Kreimer et al. (2005), who reported that HPV-related oral cancers are more frequently located in these areas, particularly the oropharynx, including the base of the tongue and soft palate. This distribution suggests that these sites might be more susceptible to HPV-related oncogenic transformation.[18]

Our findings indicate a significant relationship between lesion size and HPV positivity, with larger lesions (>1 cm) showing higher HPV prevalence. This is consistent with the study by D'Souza et al. (2016), which found that larger oral lesions, particularly those that are malignant or pre-malignant, are more likely to be HPV-positive . The statistical significance in our study (p-values of 0.032 and 0.042 for smaller and larger lesions, respectively) suggests that HPV may contribute to lesion growth and progression, particularly in the context of malignant transformation.[19]The histopathological analysis revealed a higher prevalence of HPV in malignant lesions (45%) compared to benign ones (25%). This finding is corroborated by the work of Kreimer et al. (2010), which demonstrated a strong association between HPV and oral squamous cell carcinoma, reinforcing the virus's role in oral carcinogenesis.[20] The overall HPV prevalence in our study (33%) is also comparable to the global prevalence reported in a meta-analysis by Ndiaye et al. (2014), which found an HPV prevalence of approximately 25-30% in oral cancers, further supporting the hypothesis that HPV is a significant risk factor in the development of oral malignancies .[21]

CONCLUSION

We concluded that the HPV prevalence was higher in malignant oral lesions, particularly oral squamous cell carcinoma, compared to benign lesions. Clinical presentations such as ulcers and red patches, as well as lesions located on the tongue and palate, were more likely to be associated with HPV infection. Larger lesions also showed a greater likelihood of HPV positivity. These results highlight the potential role of HPV in the development of malignant oral lesions and suggest the importance of considering HPV testing in patients with specific lesion characteristics.

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