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Orginal Article

KNOWLEDGE ABOUT ROLE OF HPV AS A RISK FACTOR OF ORAL SQUAMOUS CELL CARCINOMA AMONG DENTISTS IN ASIA. A SYSTEMIC REVIEW

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ABSTRACT

Objectives: *To assess the awareness and the knowledge among dentists of Asia about the Human Papillomavirus (HPV) as a risk factor in oral squamous cell carcinoma (OSSC).*

Materials and Methods: *This systemic review was conducted on cross-sectional and observational research to assess dentists' knowledge of HPV as a risk factor for OSCC in Asia. Up until August 9, 2024, databases including PubMed, Web of Science, Scopus, and Google Scholar were searched for relevant studies. Studies applying dentists as participants carried out in Asian nations met the eligibility requirements. The Joanne Briggs Institute (JBI) criteria for analytical cross-sectional research was used to assess the quality of the investigations.*

Results: *Studies from Asian countries, including Saudi Arabia, Turkey, Malaysia, Indonesia, and Pakistan, met the inclusion criteria. The findings revealed significant disparities in knowledge across regions. In Indonesia, 98% of dentists demonstrated a high understanding of HPV's role in OSCC, while in Pakistan and Malaysia, many dentists were unaware of this association. Gender and education level influenced awareness, with male students showing more knowledge about HPV's link to oropharyngeal cancer, while female students were better informed about HPV vaccination. These results highlight the need for enhanced education and training programs to address these gaps.*

Conclusion: *Asian nations have an increased incidence of oral squamous cell carcinoma (OSCC), with tobacco use, alcohol intake, and chewing betel quid as major risk factors. There is growing evidence that HPV, specifically subtypes HPV-16 and HPV-18, plays a major role in the development of OSCC. In Asia, dentists are still mostly unaware of the role HPV plays in OSCC risk factor education and early diagnosis, despite their critical role in this respect.*

Key words: *Knowledge, Risk Factors, HPV, OSCC*

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INTRODUCTION

In 2020, approximately 377,713 more cases of oral cancer were diagnosed world, nearly 2% accounting for of all new cancer cases, with a highest incidence rate among men . Notably, oral squamous cell carcinoma (OSCC) shows significant geographic

variation, with Asia became a site for rising incidence rates (World Health Organization, GLOBOCAN). This systematic studies shows an increasing incidence of OSCC in Asian nations particularly among younger individuals and females , with notable demographic shifts[1,2].

Tobacco use, like betel quid chewing and smoking, excessive alcohol consumption are primarily OSCC's risk factors and causes increasing rate of human papillomavirus (HPV) infection[3]. The association between oropharyngeal squamous cell carcinoma (OPSCC) and HPV is well known but its role in OSCC remains a subject of debate[4]. HPV is believed to cause carcinogenesis when HPV-DNA integrates into the host genome and leads to the production of E6 and E7 oncoproteins. These proteins inactivate p53 and pRb, that are key tumor suppressors, resulting in uncontrolled malignant transformation and cell proliferation[5,6]. However, this mechanism that contributes to OSCC, particularly in non-oropharyngeal sites, remains unclear[7].

A recent systemic review of 5,000 OSCC patients found an overall HPV prevalence of only 6% across 24 countries with the dominant subtype HPV-16 , followed by HPV-18[8]. In contrast, Asian countries have a heavy burden of OSCC, attributed to risk factors such as betel quid chewing, alcohol consumption and smoking[9,10]. Different studies suggest that betel quid chewing and smoking may facilitate HPV infection persistently, further complicating the relationship between viral and environmental carcinogens[11,12].

Recent reports show an increasing incidence of OSCC in younger individuals, especially females, with a predominance for the tongue. Some studies shows an association between tongue OSCC and HPV infection, yet the evidence is insufficient[13,14,15]. While the association between HPV and OPSCC is accepted widely , the association between HPV and OSCC is still debatable due to variations in study methodologies, discrepancies in HPV detection techniques and geographic differences.

Because of these uncertainties, a comprehensive analysis of relationship of HPV with OSCC, especially in Asian nations, is necessary. In countries such as Taiwan, China, and Southeast Asia, betel quid chewing remains important, potentially modifying HPV's role in OSCC pathogenesis[16,17]. Despite the increasing burden of OSCC, very limited research has done to explore dentists' awareness and understanding of HPV as a risk factor for OSCC. As the dentists play an important role in early detection, patient education, and risk assessment, their knowledge of HPV's potential involvement in OSCC is vital for improving preventive strategies and patient outcomes. Therefore, this systematic review aims to assess dentists' awareness of the relationship between HPV and OSCC in Asian countries, with a specific focus on Saudi Arabia, Indonesia, and Turkey.

MATERIALS AND METHODS

This systematic review is registered under the registration number CRD42024573360 with PROSPERO The article follows the guidelines provided by Methods Wizard for systematic reviews. To conduct this review, the following inclusion criteria were applied:

1. Study Design: Observational studies or cross-sectional studies that compare knowledge or awareness of HPV as a risk factor for OSCC.

2. Participants: Studies that include dentists (students or professionals) as their subjects.

3. Geographical Scope: Studies conducted in Asian countries (e.g., Pakistan, India, Malaysia).

Eligible studies were those assessing knowledge or awareness of HPV as a risk factor for OSCC among dentists. Eligible comparator groups included:

• Dentists with high knowledge versus those with low or no knowledge of HPV as a risk factor.

• Comparisons between dentists from different Asian regions or countries.

• While comparisons were encouraged, they were not mandatory if study designs did not allow them.

The primary outcome of interest was the understanding or knowledge level of HPV as a risk factor for OSCC. Studies with cross-sectional or observational study designs assessing dentist knowledge about HPV and OSCC were included. The search strategy was developed and executed by MI, SM, and WR with specific restrictions applied to publication types. The following sources were excluded: theses, books or book chapters, conference abstracts, and

articles in press. Only studies published in English were included. Duplicate results were checked by FF, SR, and ZN, and supplementary searches were conducted by ZN.

The following databases were searched from inception until August 9, 2024:

• PubMed: "Knowledge and HPV and OSCC and Dentists and Asia"

• Web of Science: ("Human Papillomavirus" OR "HPV") AND ("Oral Squamous Cell Carcinoma" OR "OSCC" OR "oral cancer") AND ("knowledge" OR "awareness" OR "understanding") AND ("dentists" OR "dental professionals") AND ("Asia" OR "Asian countries")

• Scopus: Similar Boolean search strategy as Web of Science.

Two authors (MI and FF) independently screened references against eligibility criteria. Following the title/abstract screening, full texts of the selected studies were reviewed by MI and FF, and verified by WR and ZN. Citation searches were conducted by ZN and MI. Trial registries were screened by [BLANK]. Discrepancies were resolved through consensus.

RESULT

A total of 750 studies were identified from four databases. After removing 250 duplicate records, 200 studies were excluded for various reasons (e.g., systematic reviews, book chapters, case reports, and non-relevant study types). The remaining 300 records were screened, with 150 excluded at this stage. Among the 150 studies sought for full-text retrieval, 50 could not be retrieved, leading to their exclusion. Ultimately, 100 studies met the inclusion criteria

DISCUSSION

This systematic review enhances important lack of knowledge among dental professionals regarding the role of Human Papillomavirus (HPV) across Asia as a risk factor for oral squamous cell carcinoma (OSCC). The regions such as Indonesia and Turkey has a high levels of awareness, others, including Pakistan and Malaysia, have a knowledge gap. These discrepancies enhance the need for targeted educational activities to fill the specific knowledge gaps of different populations.

This review showed a significant disparity in

Table 1: Quality Assessment through JBI checklist.

	Alqhtani et al[19]	Özdede et al[20]	Arora et al[21]	Hasibuan et al[22]	Lingam et al[23]	Al-sharif et al[24]	Roslan et al[25]	Farsi et al[26]	Keser et al[27]	Tahir et al[28]
Were the criteria for inclusion in the sample clearly defined?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the study subjects and the setting described in detail?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the exposure measured in a valid and reliable way?	Yes	Yes	Yes	Yes	Yes	N/A	Yes	Yes	Yes	Yes
Were objective, standard criteria used for measurement of the condition?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were confounding factors identified?	No	N/A	N/A	No	N/A	N/A	N/A	N/A	N/A	Yes
Were strategies to deal with confounding factors stated?	No	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Were the outcomes measured in a valid and reliable way?	Yes	Yes	Yes	N/A	Yes	Yes	Yes	Yes	Yes	Yes
Was appropriate statistical analysis used?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Over all biasness	Moderate	Moderate	Moderate	High	Moderate	High	Moderate	Moderate	Moderate	Low

HPV-OSCC awareness levels across Asian countries. Studies from Turkey and Indonesia[20,22] showed high awareness, with about 98% of Indonesian general dentists considered HPV as one of major factor to OSCC. In difference, studies from Pakistan and Malaysia[25,28] showed that a major proportion of dental professionals don't have awareness of this relation. These differences enhanced the regional disparities in dental curricula and continuing education programs contribute to inconsistencies in knowledge levels.

Gender variances in HPV-related knowledge were obvious across different studies. In an international study with students from Egypt, India, Pakistan, Saudi Arabia, the United Arab Emirates, and Sudan[23], male students have shown a greater knowledge about the link between HPV and oropharyngeal cancer (OPC), while female students had better understanding about the HPV vaccine. Similarly, a Saudi Arabian study[19] found that only 22.5% of oral health practitioners were aware of the HPV vaccine, with a considerable proportion (51.5%) unaware of the HPV-OSCC relationship.

Table 3: Comparison of awareness about use of LASER in endodontic disinfection among level of experience

Country	Author	Year	Study type	Findings
Saudi Arabia	Alqhtani et al[19]	2020	Cross-sectional	Only 38.2% of physicians reported telling their patients that HPV is a potential cause of oral cancer or OSCC, despite almost 76.5% of them identifying it as such. The majority of participants (44.6%) believed that the tongue's lateral edge was the most affected area. More than half of the participants knew that malignancies linked to HPV might be avoided with vaccinations.
Turkey	Özdede et al[20]	2020	Crosssectional	The responses of dentists did not differ statistically. Most individuals were aware that OSCC might result from HPV, and of the two groups, 75.6% said that different HPV types are the cause of OSCC 34.1% of dentists said that OSCC have a better prognosis than other OSCC that are caused by HPV.
Malaysia	Arora et al[21]	2018	Cross sectional	One hundred sixty-five individuals thought that HPV might be the cause of mouth cancer. About 43% of respondents said that treatment plans for OSCCs connected to HPV differed from those for other OSCCs.
Indonesia	Hasibuan et al[22]	2018	Cross sectional	The findings demonstrated that 98% of the 99 respondents had an adequate level of understanding regarding the function of HPV in OSCC. The clinical features of HPV associated with OSCC are widely accepted (64.6%). Seventy-seven percent of people know enough about the prognosis of HPV associated with OSCC.
India, Pakistan, Sudan, UAE, Saudi Arabia, Egypt	Lingam et al[23]	2022	Cross sectional mutinational	Compared to other year students, third- and fourth-year undergraduate students showed a greater awareness of OPC and its relationship to HPV; this difference was determined to be statistically significant ($P < 0.001$). India's dentists demonstrated a statistically substantial ($P < 0.001$) advantage over students from other nations in their awareness of HPV and its relationship to OPC.
Saudia	Al-sharif et al[24]	2024	cross-sectional	Overall, the average score of 53.44 ± 29.3 out of 100 indicated that people were generally aware of HPV-OSCC .Nonetheless, a notable knowledge gap was noted, as 53% of participants were not aware of the typical locations for HPV-OSCC. The participants exhibited a positive attitude toward their duty to educate patients about HPV-OPSCC and to promote HPV vaccination.
Malasyia	Roslan et al[25]	2024	cross-sectional	A total of 199 people participated in the study: 99 patients, 86 dental students, and 14 dental practitioners (DP). DP (85.7%) and DS (89.5%) had higher awareness of HPV than patients (26.3%). Furthermore, just 23.2% of patients knew that men might contract HPV.
Saudi Arabia	Farsi et al[26]	2020	cross-sectional	Comparatively to male students, female students knew more about OPC connected to HPV.
Turkey	Keser et al[27]	2020	cross-sectional	Among dentists, 82.7 agreed that certain HPV strains can cause mouth cancer.
Pakistan	Tahir et al[28]	2017	cross-sectional	Only 59.1% of participants accurately recognized HPV (human papilloma virus) as an oral cancer risk factor, with medical professionals being more aware of it than dental professionals (p value<0.05).

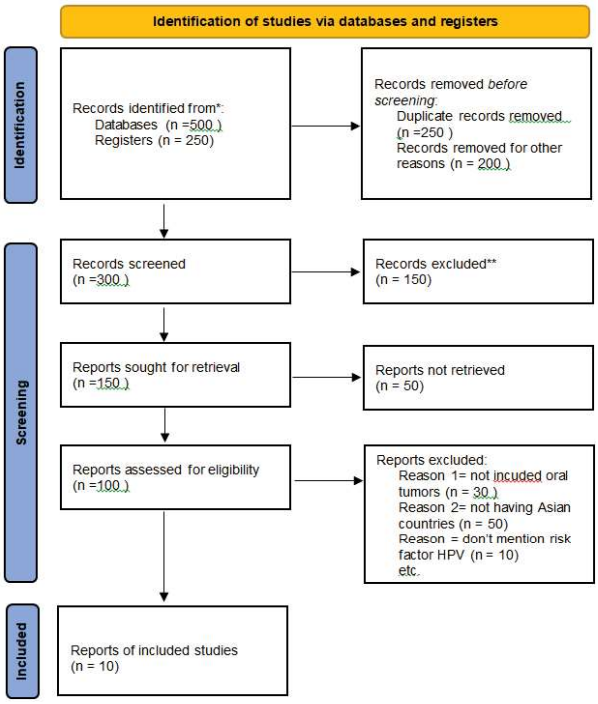

Fig 1: Prisma flow chart

These findings suggest that gender-based educational approaches may be necessary to address specific knowledge gaps effectively.

In spite of increasing evidence relating HPV to OSCC, the review found that a substantial number of dentists were not actively giving education to their patients about this risk. For instance, in Saudi Arabia[19], only 38.2% of consultants informed patients about the connection of HPV-OSCC, despite 93.1% acknowledging the need for education on the topic. Similarly, in Malaysia[28] only 41% of dentists told importance of HPV-OSCC risks to patients, and just 12% were aware of vaccine availability in the country. This shows a critical gap in patient education and highlights the need for designed training programs to equip dentists with the essential communication skills to convey HPV-related risks effectively.

The review acknowledged a need to organize standardly and region-specific educational programs to improve awareness of HPV's role in OSCC among dental professionals. A study from Saudi Arabia[26] showed that while students had an awareness score of 53.44/100, knowledge about HPV vaccination timing and OSCC locations was still lacking. Given the observed knowledge deficiencies, incorporating HPV education into undergraduate curricula, professional training, and continuing education courses is essential.

The lack of awareness of role of HPV in OSCC has major effects for both clinical practice and public health. Dental professionals play an important role in early recognition and prevention, and their knowledge directly impacts patient outcomes. Addressing these educational gaps could lead to improved screening practices, earlier diagnosis, and increased patient awareness regarding HPV prevention strategies, including vaccination.

CONCLUSION

The findings of this systematic review highlight the pressing need for improved education and awareness among dental professionals regarding HPV as a risk factor for OSCC. Despite the virus's well-documented role in oral malignancies, substantial knowledge gaps persist across different Asian regions. Addressing these deficiencies through targeted educational initiatives and professional development programs is crucial to enhancing dentists' ability to educate patients, recognize early HPV-related lesions, and advocate for preventive measures, including vaccination. Future research should focus on evaluating the effectiveness of such interventions in improving knowledge and clinical practice.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
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AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

Conception or Design:	MI, FF, SM, SAR, ZN, ZS
Acquisition, Analysis or Interpretation of Data:	MI, FF, SM, SAR, ZN, ZS
Manuscript Writing & Approval:	MI, FF, SM, SAR, ZN, ZS

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.