BMC Oral Health

SYSTEMATIC REVIEW

Open Access

Prevalence of oral HPV in healthy and lesion-bearing populations in Iran: a systematic review and meta-analysis

Mohammadreza Kashefi Baher[1*], Anahita Moscowchi[2] and Saede Atarbashi-Moghadam[3]

Abstract

Background Human papillomavirus (HPV) is a prevalent sexually transmitted virus associated with various oral lesions. While oral HPV infections are common, there is a lack of comprehensive data on its prevalence in regions like Iran. This study aims to assess the prevalence of oral HPV infection in the Iranian population, comparing healthy individuals to those with oral lesions, including oral squamous cell carcinoma (OSCC), oral potentially malignant disorders (OPMDs), and benign lesions.

Methods A systematic review and meta-analysis were conducted following PRISMA guidelines. A comprehensive search was performed across PubMed, Scopus, and Web of Science, supplemented by manual search using google scholar and observational studies (case–control, cross-sectional, and case series) were included if they reported the prevalence of oral HPV infection in Iran. Data synthesis performed to calculate pooled prevalence rates, subgroup analyses by lesion type, and HPV subtype distribution.

Results Of 85 screened studies, 48 were included in the qualitative synthesis, with 36 focused on lesion-bearing patients and 19 on healthy individuals. The overall prevalence of oral HPV infection was 18.3%, with a higher prevalence in lesion-bearing patients (27.1%) compared to healthy individuals (8.2%). The highest prevalence was observed in patients with OSCC (22.7%) and OPMDs (31.2%). HPV-16 was the most common subtype in both groups. A meta-regression analysis revealed a significant association between female sex and HPV detection. Comparative analysis showed significantly higher odds of HPV detection in individuals with oral lesions (OR = 4.78).

Conclusions Oral HPV infection is significantly more prevalent in individuals with oral lesions, especially for HPV-16 and HPV-18. This highlights the importance of HPV in oral health and underscores the need for multidisciplinary efforts to optimize interventions and reduce HPV-related oral disease burden, particularly in regions like Iran.

Trial registration This study is registered with PROSPERO (Registration No. CRD42025641087).

Keywords Human papillomavirus viruses, Iran, Oral, Squamous cell carcinoma, Lichen planus, Polymerase chain reaction

*Correspondence:
Mohammadreza Kashefi Baher
rezakashefi78@gmail.com
[1] Health Research Center, Chamran Hospital, Tehran, Iran
[2] Dental Research Center, Research Institute for Dental Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[3] Department of Oral and Maxillofacial Pathology, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background

Human papillomavirus (HPV), a double-stranded DNA virus, is the most common sexually transmitted virus worldwide, primarily causing infections of the skin and mucosal surfaces [1, 2]. HPVs are resistant to numerous disinfectants and are relatively unaffected by environmental factors. The beta, gamma, mu, and Nu types of

HPV lead to infections of the epidermis, and alpha-HPV is responsible for infections in both the epidermal and mucosal epithelial tissues [3].

While the prevalence of genital HPV has been reported globally to be 31% in men and 11.5% in women, higher rates may be observed among more sexually active individuals [4, 5]. Importantly, HPV is not only associated with genital infections but also associated with various cancers, including cervical, penile, vulvar, vaginal, anal, and oropharyngeal cancers (highlighting the importance of HPV infection assessment in the oral cavity). Among the estimated 12.7 million cancer cases worldwide in 2008, approximately 610,000 were attributable to HPV [5]. The entry point for infection is through a wound or microdamage to the epithelium, which enables the virus to access the basal layer. HPV is capable of infecting only the dividing keratinocytes of the basal layer, such as those involved in the healing process of an injury. Papillomaviruses can remain in a latent state even after the disease has resolved, leading to occasional recurrences [6].

Approximately 30 HPV subtypes can infect the oral mucosa, contributing to various conditions ranging from subclinical infection to lesions such as squamous papilloma, condyloma acuminatum, verruca vulgaris, multifocal epithelial hyperplasia, squamous cell carcinoma, and verrucous carcinoma [7–9]. HPV is linked to a range of benign, potentially malignant, and malignant epithelial lesions; however, the majority of infected individuals remain asymptomatic and do not exhibit any clinically noticeable disease. The clinically significant HPVs, which encompass both high-risk mucosal types such as HPV16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82 and low-risk mucosal types such as HPV6, 11, 40, 42, 44, 54, 55, 61, 62, 71, 74, 81, 84, 89 (CP6108), 90, along with skin-wart-causing strains such as HPV1, 2, 3, 7, 10, 27, 57, 73, are categorized as alphapapillomaviruses [3].

Despite this, there is a lack of updated evidence on the prevalence of oral HPV infection, particularly in regions such as Iran. For example, an estimated 7.3% of the U.S. population has detectable oral HPV, with 3.1% testing positive for oncogenic types [10]. Current vaccines are prophylactic rather than therapeutic [6]. At present, there is no medication to prevent viral replication, and treatment relies on lesion removal or stimulation of the host immune system [3]. Since similar data from Iran are scarce, understanding the full scope of oral HPV infection prevalence and its potential health implications remains challenging. Elucidating the prevalence of oral HPV infection in the Iranian population is clinically significant for guiding public health strategies, vaccination policies, and improving early detection efforts for HPV-associated oral lesions, including oropharyngeal cancers.

Given this knowledge gap, we aimed to conduct a systematic review and meta-analysis to assess the prevalence of oral HPV infection in the Iranian population and compare it between healthy individuals and lesion-bearing patients, as well as among different lesion types, including oral squamous cell carcinoma (OSCC), oral potentially malignant disorders (OPMDs), and benign lesions.

Methods

Study design and guidelines

This systematic review follows the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [11] and is registered with the International Prospective Register of Systematic Reviews (PROSPERO; Registration Number: CRD42025641087).

Research question and eligibility criteria

The research question was structured via the PEOS (population, exposure, outcome, study design) framework [12] to assess and compare the prevalence of oral HPV infection in the Iranian population. It focused on Iranian individuals, including both lesion-bearing and healthy individuals, with the presence of oral lesions as the exposure and the prevalence of oral HPV as the outcome. Eligible studies, were observational in design, including case–control, cross–sectional, and case series studies.

Information sources and search strategy

A comprehensive systematic search was performed in PubMed, Scopus, and Web of Science, complemented by a manual search using Google Scholar, with no restrictions on language or publication date, and the last search was conducted on February 6, 2025. Additionally, to increase the validity of the search, the reference lists of all the included studies were manually searched to identify any potential additional sources for inclusion.

The search strategy focused on four key concepts using the terms "Oral" and "(HPV or human papillomavirus)" and "(prevalence or epidemiology or incidence)" and "(Iran or Persian). The detailed search terms are provided in Supplementary Table 1 (see Additional file 1).

Study selection process

The study selection process followed a structured four-phase approach managed via EndNote reference software. Initially, duplicate records were removed both automatically and through manual evaluation. In the next phase, the titles were screened for relevance based on the eligibility criteria. The abstracts of the selected studies were then assessed for further relevance, followed by a full-text review of the remaining studies. The screening process was independently conducted by two reviewers,

with disagreements resolved through consultation with a third reviewer. (M.K.B. and A.M.)

Data collection process and data items

Data extraction sheets were used to collect the following details: first author, year of publication, study design, age (range and average), gender, sample size, location in Iran, study population, HPV detection methods, overall oral HPV prevalence, and prevalence of each HPV genotype. Two reviewers independently performed the data extraction process. (M.K.B. and A.M.)

Quality assessment

The quality assessment was conducted via tools tailored to the study design. For descriptive studies, including case–control and cross-sectional designs, the Newcastle–Ottawa Scale (NOS) was utilized [13]. Studies were classified as high quality (7 to 9 points), moderate quality (4 to 6 points), or low quality (0 to 3 points). Each study received a score to ensure a thorough evaluation of its quality and to detect any potential bias. The quality assessment was performed independently by two reviewers. (M.K.B. and A.M.)

Participant categorization

We categorized the participants in the included studies into groups of healthy individuals and patients with oral lesions, including oral squamous cell carcinoma (OSCC), oral potentially malignant disorders (OPMDs), and benign lesions. OPMDs include a group of conditions, including leukoplakia, oral lichen planus (OLP), and lesions with observed dysplasia that affect the oral mucosa and increase the risk of malignancy [14]. Healthy participants were selected from the control arms of case–control studies, as well as from cross-sectional studies that specifically evaluated healthy populations. For individuals with oral lesions, the data were obtained from the case arms of case–control studies or from cross-sectional studies that focused on the same types of lesions as those examined in the case groups.

Data synthesis

An overall analysis was conducted to evaluate the event rate, complemented by a subgroup analysis that distinguished between cases sampled from healthy regions and those from areas with lesions, using data derived from both cross-sectional and case–control studies. Additionally, a separate subgroup analysis was carried out for HPV subtypes in relation to healthy and lesioned areas. Importantly, the pooled event rates for various HPV subtypes were derived from studies that initially confirmed the presence of oral HPV, followed by a detailed analysis of each subtype. Therefore, studies reporting a zero prevalence of oral HPV without any subtype determination were excluded from this analysis.

For the comparative analysis of HPV rates in healthy versus lesioned regions, data from case–control studies were employed and reported as odds ratios with 95% confidence intervals (CIs). The results are presented without consideration of subtype, accompanied by subgroup analysis categorized by subtype.

In instances where the number of detected cases was zero, a continuity correction was automatically applied; to increase the accuracy of the results, the Mantel–Haenszel method was subsequently utilized to adjust the findings, as recommended [15].

The assessment of heterogeneity across the studies was conducted with the chi-square-based Q test. A p value exceeding 0.10 was interpreted as an absence of significant heterogeneity. In cases of significant heterogeneity, a random-effects model was implemented; conversely, a fixed-effects model was adopted when heterogeneity was not significant. The risk of publication bias was assessed via a funnel plot and Egger's test (the significance level was set at 0.10). In addition, a meta-regression utilizing a random-effects model was performed to examine the influence of sex on the rate of HPV detection in retrieved samples. All the statistical analyses were executed via Comprehensive Metanalysis software/Version 3 (Biostat Inc., NJ, USA), with a significance threshold of 0.05.

Results

Study selection

Through our systematic search, we identified 36 studies from PubMed, 26 from Scopus, and 25 from Web of Science. We also conducted a manual search on Google Scholar, which yielded 19 additional studies. After removing duplicates, 85 unique studies were screened. Of these, 19 were excluded based on their titles, 11 were excluded after abstract review, and 6 were excluded following full-text review due to having irrelevant outcomes (focusing on non-oral HPV infections), not specifying oral lesions, or lacking methodological quality. Additionally, one study was excluded because of the unavailability of the full text [16]. Ultimately, 48 records were included in the qualitative synthesis. Table 1 shows the characteristics of the included studies. Furthermore, to ensure a more accurate and precise meta-analysis, we excluded 9 studies. These studies were omitted either because their reported HPV prevalence included the oral area but did not focus exclusively on it or because of inappropriate case selection (such as case series studies [17, 18]), which was not ideal for inclusion in the quantitative synthesis. The detailed flow diagram is shown in Fig. 1.

Table 1 Characteristics of included studies

First Author **Year / Design**	*Age*	*Gender*	*Oral Related Sample Size*	*Location*	*Study Population*	*HPV Detection Method*	*Overall Oral HPV Prevalence (%)*	*Prevalence of Each Genotype of Oral HPV (%)*
Akhondnezhad 2018 / CS [19]	8–83 years (mean: 46.2)	48.1% F, 51.9% M	83	Mazandaran	Patients with oral tumors (SCC, papilloma, hyperplasia, dysplasia, neoplasia)	PCR	13.20%	HPV-6 = 4 (36.3%), HPV-18 = 3 (27.2%), HPV-31 = 2 (18.1%), HPV-16 = 1 (9.1%), HPV-33 = 1 (9.1%)
Abbas 2012 / CC [20]	Not specified	Not specified	total of 40, (10 mild dysplastic lesions, 10 moderate dysplastic lesions, 10 severe dysplastic lesions, 10 mucoceles)	Tehran	Patients with dysplastic lesions (mild, moderate, severe) and with a diagnosis of mucocele	PCR	37.5% overall, 40% in mucocele, 60% in mild dysplasia, 20% in moderate dysplasia, and 30% in severe dysplasia (mean in dysplastic lesions: 36.6%)	Not specified
Allameh 2018 / CC [21]	cases: 59.8 ± 13.6, controls: 44.1 ± 13.5	cases: 39 M / 28 F, controls: 35 M / 24 F	cases: 67, controls: 59	Tehran	Patients with and without OSCC	PCR	OSCC: 14.9%, control: 6.8%	HPV-16,18: 14.9% in cases
Amoli 2022 / CS [22]	39.5% under 50 y.o, 43.8% aged between 51 to 69, 16.7% over 70 y.o	45 M / 69 F	114 (33 OSCC, 28 OLP, 16 Dysplasia, 37 Irritation Fibroma)	Mazandaran	patients with oral SCC, OPMDs, and benign lesions	PCR	total: 25.4% / OSCC = 9 (27.2%) / OLP = 9 (32.1%) / Dysplasia = 2 (12.5%) / IF = 9 (24.3%)	HPV-16 and HPV-18: 0%, other genotypes not specified
Arbabi-Kalati, 2014 / CS [23]	smoking group: 43.1 ± 9.5, nonsmoking group: 42.4 ± 10	100% M	100 (50 smokers, 50 non-smokers)	Zahedan	Healthy adult men (smokers and non-smokers)	PCR	0%	HPV-16: 0%, HPV-18: 0%
Ashraf 2017 / CC [24]	27–86 years, cases: (57.36 ± 12.18), controls: (49.72 ± 10.10)	case: 36% M, 64% F / control: 46% M, 54% F	50 cases, 50 controls	Shiraz	Patients with and without oral tongue SCC	PCR	14% in cases, 0% in controls	HPV-16: 0%, HPV-18: 0% (in both cases and controls)
Azad 2006 / CC [25]	16 to 55 years old	Not specified	150 (100 intraosseous ameloblastoma, 50 controls)	Tehran	Patients with and without intraosseous ameloblastoma	PCR	32% in cases, 10% in controls	cases: HPV-6: 10 (10%), HPV-11: 4 (4%), HPV-16: 4(4%), HPV-31: 1 (1%), HPV-18: 0%, HPV33: 0% / controls: not specified
Azmoudeh 2024 / CS [26]	61–70 years (mean. 64)	18 M / 20 F	38	Qazvin	Patients with OSCC	PCR	34.20%	HPV-16: 21.0%, HPV-18: 10.5%, Others: 2.6%
Dayyani 2021 / CS [27]	Mean: 57.3 years	52.5% M, 47.5% F	63	Tehran	Patients with OSCC	PCR	6.3% (4 in 63 OSCC samples)	HPV-18: 6.3%, HPV-31: 0%

Table 1 (continued)

First Author Year / Design	*Age*	*Gender*	*Oral Related Sample Size*	*Location*	*Study Population*	*HPV Detection Method*	*Overall Oral HPV Prevalence (%)*	*Prevalence of Each Genotype of Oral HPV (%)*
Delavarian 2010 / CS [28]	20–38 years (mean: 30)	12 M / 9 F	21	Mashhad	Patients with oral SCC	PCR	0%	0%
Falaki 2009 / Case series [18]	9–43 years (mean: 16.7)	2 M / 5 F	7	Mashhad	Patients with Heck's disease	PCR	100%	HPV-13: 71.4%, HPV-32: 14.3%, HPV-16: 0%, HPV-18: 0%
Falaki 2011 / CS [29]	20–40 years (mean: 30.19)	12 M / 9 F	21	Mashhad	Patients with OSCC	PCR	0%	0%
Farhadi 2020 / CC [30]	43.8 ± 2.78 years	21 F / 11 M	32 OLP, 20 control	Tehran	Patients with and without OLP	PCR	25% in OLP, 0% in control	HPV-33: 6 (21.87%) in OLP, HPV-18: 1 (3.12%) in OLP
Habibi 2024 / CC [31]	28–90 years (avg. 53.66)	65% M, 35% F	200 (100 with oral cancer, 100 healthy patients)	Shiraz	OSCC patients and healthy controls	PCR	14% in cancer cases, 2% in controls	Not specified
Haddadi 2024 / CS [32]	under 20 to 70 years old	98% F, 2% M	total of 950 samples of which 2 of them were oral	Kurdistan	Various samples (oral, vaginal, etc.)	PCR	100% (there were two oral samples, both with positive HPV tests)	Not specified
Haghighat 2019 / CS [33]	42.92 ± 18.84 years	181 M / 262 F	443	Shiraz	Patients with non-odontogenic oral mucosal infectious lesions	PCR	7.70%	Not specified
Halimi 2011 / CS [34]	68.9	18 M / 12 F	30 oral SCC, (and 30 lung SCC)	East Azerbaijan	Patients with oral and lung squamous cell carcinoma	PCR	20% for oral SCC	Not specified
Haratian 2010 / CC [35]	FA group: 9.9 ± 3.9 years, Non-FA group: 44.37 ± 13.7 years	FA: 59% M, Non-FA: 50% M	22 (FA) + 24 (non-FA)	Tehran	Patients with HNSCC, including FA patients	PCR	71.70%	HPV-16: 73.9%, HPV-18: 26%, HPV-31: 19.6%
Jahanshahi 2005 / CS [36]	34–80 years (63.97 avg)	25 M / 17 F	42 (36 OSCC, 6 VC)	Isfahan	Patients with oral SCC and VC	PCR	50%	HPV-16,18 together: 26.2%
Karbalaie Niya 2017 / CS [37]	28–86 years (mean: 60.5)	121 M / 35 F	156	Tehran	Patients with HNSCC	PCR	3.2% in all lesions	HPV-16: 1.3%, HPV-2: 0.6%, HPV-27,43: 1.3%

Table 1 (continued)

First Author Year / Design	*Age*	*Gender*	*Oral Related Sample Size*	*Location*	*Study Population*	*HPV Detection Method*	*Overall Oral HPV Prevalence (%)*	*Prevalence of Each Genotype of Oral HPV (%)*
Karimi 2022 / CC [38]	control: 54.3, case: 57.4	75.7% M, 24.3% F	498 HNSCC cases, 242 controls	Iran (multi-center)	Patients with HNSCC	PCR		α-HPV: 1.2% in cases, 2.9% in controls/ β-HPV: 43.8% in cases, 38.6% in controls/ γ-HPV: 26.1% in cases, 24.9% in controls
Karimi 2024 / CC [39]	Not specified, but matched by age (± 5 years)	Not specified	498 cases, 242 controls	Iran (multi-center)	Patients with and without HNSCC	PCR	1.2% α-HPV, higher β- and γ-HPV prevalence in both groups	α-HPV: 4.6%, β-HPV: HPV23, γ-HPV: HPV134 prevalent
Kermani 2012 / CC [40]	cases: 27–50 years (mean: 39.71), controls: 18–50 (mean: 32.9)	6 M / 8 F (cases), 43 M / 49 F (controls)	14 patients (5 OSCC), 94 controls	East Azerbaijan	Patients with and without HNSCC	PCR	Cases: 57.1% (40% for OSCC), Controls: 5.4%	Cases: HPV-18: 28.6%, HPV-16: 14.3%, HPV-6 (low risk): 14.3% / Controls: 4.3% HPV-18, 1.1% HPV-6, 0% HPV-16
Khalesi 2023 / CS [41]	Avg. 59.7 years	47.5% M, 52.5% F	40	Isfahan	Patients with OSCC	P16	90% positive for p16 (HPV marker)	Not specified
Makvandi 2022 / CS [42]	53.23 ± 15.19 years	87 (52.4%) M, 79 (47.6%) F	166	Ahvaz	Patients with oral and oropharynx SCC	PCR	16.40%	HPV-16: 2.14%
Mohammadi 2023 / CC [43]	controls: 44.08 ± 4.28, cases: 48.28 ± 6.33	cases: 12 (48%) M, 13 (52%) F / control: 13 (52%) M, 12 (48%) F	50 (25 OLP, 25 control)	Birjand	Patients with and without OLP	PCR	56% in cases, 28% in controls	HPV-16: 48% in cases and 24% in controls, HPV-18: 12% in cases and 4% in controls, HPV-16–18 together: 56% in cases and 28% in controls
Moshiri 2016 / CS [44]	17–91 years (mean: 62.5)	71% M, 29% F	104 were enrolled but 24 related to upper-third esophageal epithelium	Mazandaran	patients with non-cancerous upper-third esophageal lesions	PCR	45.80%	Not specified
Moshref 2009 / CS [45]	25–93 years (mean: 58.4)	19 M / 21 F	40	Tehran	Patients with OSCC	PCR	25%	HPV-16: 20%, HPV-18: 7.5%
Mozaffari 2010 / Case series [17]	8–43 years (mean: 19.50)	5 M / 7 F	12	Mashhad	Patients with MEH	PCR	100% (in 7 patients that were analyzed for HPV)	HPV-13: 71.4%, HPV-32: 14.3% (reported percentages based on 7 samples that underwent HPV assessment)

Table 1 (continued)

First Author Year / Design	*Age*	*Gender*	*Oral Related Sample Size*	*Location*	*Study Population*	*HPV Detection Method*	*Overall Oral HPV Prevalence (%)*	*Prevalence of Each Genotype of Oral HPV (%)*
Namin 2003 / CC [46]	16–51 (mean: 31.8 ± 2.46)	26 M / 24 F (similar in both cases and controls)	50 Ameloblastomas, 50 Controls	Tehran	Patients with and without Ameloblastoma	PCR	40% of the cases, 18% of the controls	HPV-6 in cases: 16% / HPV-8,11,16,18,31,33: 0% (in both cases and controls), all the other positive HPVs were unidentified, but they were not among the 7 high-risk HPV categories
Nikakhlagh 2012 / CS [47]	Average 67.2 years	151 (85.8%) M, 25 (14.2%) F	176	Ahvaz	Patients with HNSCC	PCR	3.90%	HPV-16: 1.7%, HPV-18: 1.1%, HPV-57: 0.6%, HPV-33: 0.5%
Nili 2023 / CS [48]	63.0 (mean)	10 M / 9 F	19 (a total of 331 samples from different body parts)	Tehran	Patients with SCC	Koilocyte	36.8%	Not specified
Pouide 2016 / CS [49]	15 to 75 y.o	35 M / 35 F	70	Tehran	Patients with OSCC	PCR	11.40%	HPV-6: 4.3%, HPV-16: 7.1%
Rahbarnia 2019 / CC [50]	32–88 years (mean: 61.26)	15 M / 15 F	30 patients, 30 controls	East Azerbaijan	Patients with and without OSCC	PCR	10% in cases, 0% in controls (healthy saliva samples)	Not specified
Razavi Nikoo 2017 / CC [51]	Not specified	Not specified	50 cases, 10 controls	Tehran	Patients with and without OSCC	PCR	36% in cases	Cases: HPV-18: 20%, HPV-11: 16%
Razavi 2009 / CC [52]	22–84 years (Mean: 49)	24 M / 19 F	43 (29 cases, 14 controls)	Isfahan	Patients with and without OLP	PCR	31% in cases, 7.1% in controls	HPV-18: 31% in cases, 7.1% in controls
Rezaei 2021 / CS [53]	61.67 ± 14.41 years	26 M / 20 F	46	Tehran	Patients with OSCC	PCR	6.50%	HPV-18: 4.3%, HPV-52: 6.5%, HPV-61: 4.3%, HPV-67: 2.2%, HPV-73: 2.2%
Saghravanian 2015 / CC [54]	19–85 years (Mean: 59 y.o, approximately)	90 M / 83 F	173 (114 SCCs, 21 VCs, 20 Leukoplakia, and 18 normal mucosal)	Mashhad	Patients with OSCC, verrucous carcinoma, leukoplakia, and normal mucosa	PCR	10.4% (all in SCC and VC), 13.1% in SCC, 14.3 in VC, 0% in leukoplakia, 0% in normal mucosa	OSCC: HPV-6: 6.7%, HPV-11: 33.3%, HPV-6 & 11: 13.3%, HPV16,18, 31,33: 0%, 46.7% were undetermined HPV subtypes / VC: HPV-16: 14.3%, HPV-18: 14.3%

Table 1 (continued)

First Author Year / Design	*Age*	*Gender*	*Oral Related Sample Size*	*Location*	*Study Population*	*HPV Detection Method*	*Overall Oral HPV Prevalence (%)*	*Prevalence of Each Genotype of Oral HPV (%)*
Sahebjamiee 2009 / CC [55]	cases: 64.2 ± 14.9 years, controls: 64.4 ± 15	cases: 9 M / 13 F, controls: 8 M / 12 F	22 patients, 20 controls	Tehran	Patients with and without OSCC	PCR	40.9% in cases, 25% in controls	controls: HPV-6/11: 5%, HPV-16: 20%, HPV-18: 0%, HPV-31/33: 0%, cases: HPV-6/11: 16.6%, HPV-16: 27.3%, HPV-18: 4.5%, HPV-31/33: 0%
Sahebjamiee 2015 / CC [56]	53 ± 12.5 years	16 M / 64 F	total of 80, 40 (patients), 40 (controls)	Tehran	Patients with and without OLP	PCR	27.5% in OLP tissue, 7.5% in OLP saliva, 12.5% in healthy saliva	HPV-16: 12.5% in OLP tissue and healthy saliva, HPV-18: 7.5% in OLP tissue; HPV-16: 2.5% in OLP saliva, HPV-18: 5% in OLP saliva and 0% in healthy saliva
Salehi 2013 / CC [57]	18–83 years (Mean: 55 y.o, approximately)	18 M / 22 F	40 (10 leukoplakia, 10 OHL, 10 mild dysplasia, 10 Healthy)	Rasht	Patients with leukoplakia, OHL, mild dysplasia, or healthy samples	PCR	leukoplakia: 70%, OHL: 70%, mild dysplasia: 10%, healthy: 10%	leukoplakia: 30% HPV-11, 0% HPV-18, 0% HPV-16 / OHL: 20% HPV-11, 20% HPV-18, 10% HPV-16 / mild dysplasia: 0% HPV-11, 0% HPV-18, 0% HPV-16 / healthy: 10% HPV-11, 0% HPV-18, 0% HPV-16
Sargolzaei 2005 / CC [58]	56.6	Not specified	51 oral SCC, 28 controls	Zahedan	Patients with and without OSCC	PCR	21.5% in the cases and 3.6% in the controls	in cases: HPV-6: 7.8%, HPV-31: 5.8%, HPV-33: 1.9%, HPV-35: 1.9%, HPV-11:0%
Seifi 2013 / CS [59]	16–61 years (mean: 31.61)	52 M / 53 F / 9 unknown	114	East Azerbaijan	Healthy individuals (cancer-free individuals)	PCR	6.10%	HPV-18: 4.4%, HPV-6: 0.85%, HPV-66: 0.88%
Seraj 2011 / CS [60]	22–84 years (mean: 57.88)	51 M / 43 F	94	Tehran, Mashhad	Patients with oral tongue SCC	PCR	26.60%	HPV-16: 10.6%, HPV-18: 16%, HPV-16,18 together: 0%
Tabatabai 2015 / CC [61]	cases: 25–81 years (mean: 64.2) / controls: 22–78 years (mean: 63.6)	cases: 22 M / 17 F, controls: 18 M / 9 F	39 patients, 27 controls	Yazd	Patients with and without OSCC	PCR	43.6% in cases, 0% in controls	cases: HPV-16: 43.6%, HPV-18: 12.8%, HPV 16–18: 12.8% / controls: 0% for HPV 16 and 18

Table 1 (continued)

First Author Year / Design	*Age*	*Gender*	*Oral Related Sample Size*	*Location*	*Study Population*	*HPV Detection Method*	*Overall Oral HPV Prevalence (%)*	*Prevalence of Each Genotype of Oral HPV (%)*
Yahyapour 2013 / CS [62]	67.6 ± 9.7 for upper-third esophageal SCC	27 M / 19 F (for upper third esophageal SCC)	46 upper-third esophageal SCC (excluding middle and lower-third esophageal SCC)	Mazandaran	patients with upper-third esophageal SCC	PCR	28.30%	HPV-6: 2.2%, HPV-31: 2.2%, HPV-33: 2.2%, HPV-45: 2.2%, HPV-52: 2.2%, HPV-16:0%, HPV-11:0%, HPV-18:0%
Zarei 2007 / CS [63]	4–74 years (mean: 43)	36 M / 24 F	total of 60, (OSCC: 15, Leukoplakia: 15, OLP: 15, PG: 15)	Kerman	Patients with OSCC, leukoplakia, OLP, and PG	PCR	OSCC: 60%, Leukoplakia: 26.7%, OLP: 13.3%, PG: 6.7%	OSCC: HPV-16: 40%, HPV-18: 20% / Leukoplakia: HPV-16: 13.3%, HPV-11: 13.3% / OLP: HPV-6: 13.3% / PG: HPV-11: 6.7%
Zargaran 2020 / CS [64]	19–65 years (mean: 36.03)	157 M / 143 F	300	Kurdistan	Healthy individuals	PCR	12%	HPV-6: 0.67%, HPV-53: 0.33%

CC Case–Control, *CS* Cross-Sectional, *OSCC* Oral Squamous Cell Carcinoma, *HNSCC* Head and Neck SCC, *OHL* Oral Hairy Leukoplakia, *IF* Irritation Fibroma, *PG* Pyogenic Granuloma, *OLP* Oral Lichen Planus, *OPMDs* Oral Potentially Malignant Disorders, *NOS* Newcastle–Ottawa Scale, *MEH* Multifocal Epithelial Hyperplasia, *PCR* Polymerase chain reaction

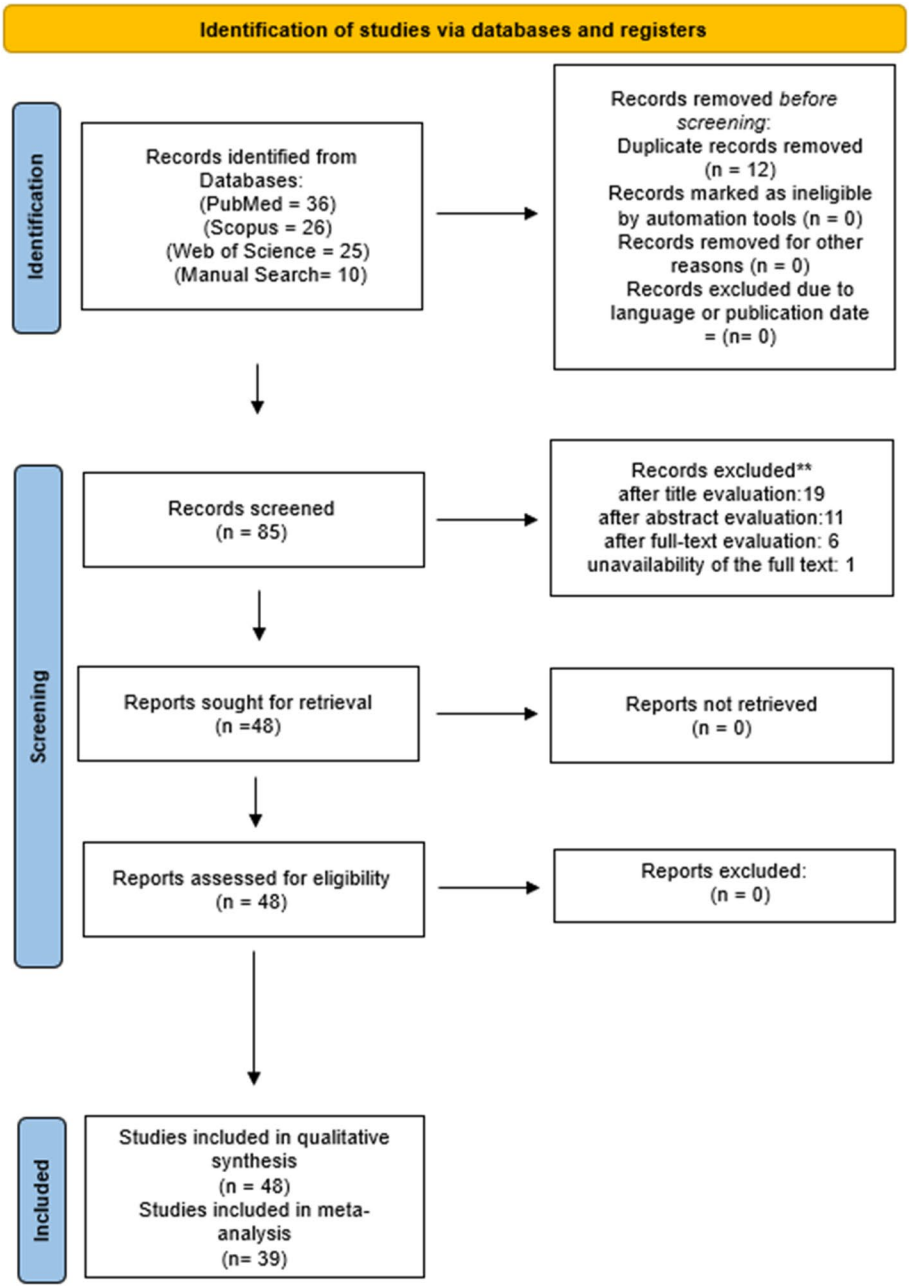

Fig. 1 Flow diagram of the systematic search

Study characteristics

A total of 48 studies were included in the qualitative analysis, with case–control ($n=21$; 43.75%), cross–sectional ($n=25$; 52.08%), and case series ($n=2$; 4.16%) designs. All included studies were published between 2003 and 2024, even though no restrictions were placed on the publication year. The sample sizes of the included studies ranged from 7 participants in the Falaki et al. [18] study to 740 in the Karimi et al. study [38]. All studies were conducted in Iran, with the highest number from Tehran (33.3%), followed by Mashhad (12.5%), including one study conducted across both Tehran and Mashhad [60]. The contributions from Mazandaran, Azerbaijan, and East Azerbaijan were 8.3% each, whereas those from Shiraz and Isfahan represented 6.2% each. Ahvaz, Zahedan, and Kurdistan contributed 4.2% each. Yazd, Qazvin, Rasht, Birjand, and Kerman each accounted for 2.1%. Additionally, 4.2% of the studies were multicenter investigations.

Both case series studies demonstrated the strongest possible link between oral HPV infection and multifocal epithelial hyperplasia (Heck's disease), reporting a 100% prevalence of oral HPV in these lesions [17, 18].

HPV detection methods predominantly utilize PCR (95.83%) to identify HPV-positive samples. However, alternative methods were also employed, with one study [41] using p16 immunohistochemistry (2.08%) and one study (2.08%) relying on the identification of koilocytes [48], a cytological marker of HPV infection.

Quality assessment

We applied the Newcastle–Ottawa Scale (NOS) for quality assessment and determined that none of the included studies were of low quality. The NOS scores ranged from 4.5 to 7, with a mean score of 5.79, indicating that, on average, the studies fell into the moderate-quality category.

Lesion-based study categorization

We classified the participants in the included studies into groups of healthy individuals and patients with oral lesions. In this review, 19 and 36 eligible studies provided evaluable data on the prevalence of oral HPV infection in healthy individuals (without lesions) and lesion-bearing patients, respectively. Among the studies that included individuals with oral lesions, 24 focused on OSCC, 9 focused on OPMDs (6 focused on OLPs and 5 focused on premalignant lesions, 2 of which were both OLP and premalignant lesions), and 7 focused on benign oral lesions, all of which provided analyzable data for the prevalence of oral HPV.

Sex-based analysis of oral HPV infection

Nineteen studies reported oral HPV-positive samples categorized by sex, with the proportion of female cases among HPV-positive individuals ranging from 0% in the study by Rezaei et al. [53] to 71.43% in the study by Seifi et al. [59]. A meta-regression analysis via a random effects model revealed a significant direct association between female sex and the number of HPV-positive cases (coefficient: 0.08, 95% CI: 0.02 to 0.14; $P=0.012$). Conversely, a nonsignificant inverse correlation was observed for male sex (coefficient: −0.02, 95% CI: −0.08 to 0.03, $P=0.395$).

Overall HPV analysis

The random effects model meta-analysis revealed that the prevalence of oral HPV infection in the oral cavity among the Iranian population, irrespective of the presence or absence of lesions, was 18.3% (95% CI: 14.8%–22.3%). Among individuals without lesions, the prevalence decreased to 8.2% (95% CI: 5.6%–12.0%), whereas in lesion-bearing patients (regardless of lesion type), it increased to 27.1% (95% CI: 21.3%–33.6%) (see Additional file 2). Furthermore, the prevalence of oral HPV was 22.7% (95% CI: 20.2%–25.4%) in patients with OSCC (Fig. 2) and 31.2% (95% CI: 23.1%–0.40.6%) in patients with OPMDs. Specifically, for oral lichen planus, a prevalence of 32% (95% CI: 21.8%–44.1%) was achieved. Additionally, the prevalence of HPV in benign oral lesions was 27.3% (95% CI: 13.3%–0.47.9%).

HPV subtype analysis

The analysis of oral HPV subtypes in individuals without lesions revealed the following results: among high-risk subtypes, HPV-16 had a pooled event rate of 4.9% (95% CI: 1.8%–12.8%), whereas HPV-18 had an event rate of 3.4% (95% CI: 2.0%–5.6%). Among the low-risk subtypes, HPV-6 had a pooled event rate of 0.8% (95% CI: 0.3%–2.1%), and HPV-11 had an event rate of 4.5% (95% CI: 0.9%–19.8%). In lesion-bearing patients, with respect to high-risk subtypes, HPV-16 had a pooled event rate of 9% (95% CI: 5.0%–15.7%), and HPV-18 had an event rate of 7.6% (95% CI: 5.0%–11.5%). For the low-risk subtypes, the prevalence of HPV-6 was 7% (95% CI: 4.8%–10.0%), and that of HPV-11 was 6% (95% CI: 2.7%–12.9%). Furthermore, HPV-31 was detected in 2.6% of patients with lesions (95% CI: 1.2%–5.5%), whereas HPV-33 was detected in 2.4% (95% CI: 0.4%–13.9%). Overall, HPV-16 is the most common HPV subtype detected in both healthy individuals and lesion-bearing patients. Table 2 shows the assessments of different HPV subtypes, including the number of related studies, pooled event rate, meta-analysis model, and level of heterogeneity.

HPV comparative analysis

A fixed-effect model meta-analysis revealed that the likelihood of detecting oral HPV was significantly greater in patients with oral lesions than in healthy individuals (P value <0.001), with an odds ratio (OR) of 4.78 (95% CI: 3.286–6.951) (Fig. 3). Additionally, the presence of oral lesions increased the odds of detecting HPV-16 by 2.72-fold (OR = 2.720, 95% CI: 1.442–5.130; P value = 0.002). Moreover, the odds of detecting HPV-18 in the oral cavity increased by 4.79 times (OR = 4.788, 95% CI: 1.607–14.269; P value = 0.005) in the presence of lesions, regardless of lesion type (Fig. 4).

Publication bias

The results of Egger's test demonstrated that the overall HPV analysis indicated no evidence of publication bias (P-value = 0.307). However, the comparative HPV analysis revealed significant publication bias (P-value = 0.00064). Figure 5 demonstrates the funnel plots of both the overall and comparative HPV analysis.

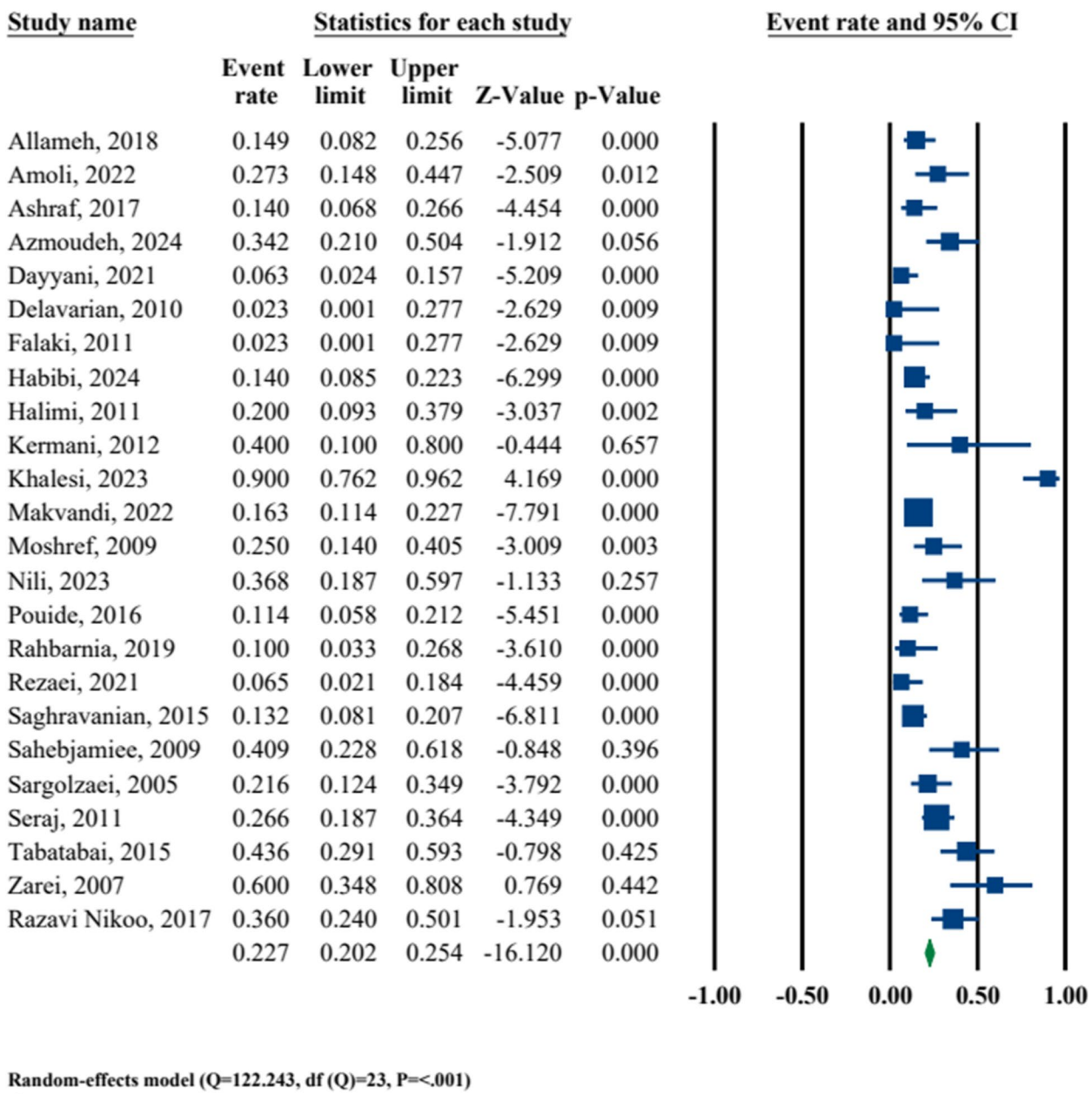

Fig. 2 Forest plot of the meta-analysis conducted on studies that reported the prevalence of oral HPV in patients with OSCC

Discussion

This systematic review and meta-analysis sought to investigate the prevalence of oral HPV infection in the Iranian population. The findings revealed an overall oral HPV prevalence of 18.3%. HPV is more prevalent in the presence of oral lesions than in the absence of lesions. Among the various types of lesions, OLP, a category of OPMDs, has the highest oral HPV prevalence, followed by OSCC and, subsequently, benign lesions. The prevalence of each HPV subtype is greater in patients with oral lesions, with HPV-16 being the most common subtype identified in both healthy individuals and those with lesions. This study further revealed that the presence of oral lesions significantly elevates the likelihood of HPV detection, with an increase in odds exceeding 4.5-fold. Specifically, for high-risk HPV subtypes, the presence of oral lesions increased the odds of detecting HPV16 by 2.7-fold and HPV18 by 4.8-fold.

Table 2 Pooled event rate of different HPV subtypes in both healthy individuals and lesion-bearing patients

	HPV subtype	Number of studies	Pooled event rate	95% confidence interval	Model	Heterogeneity			
						Q-value	df (Q)	*P* value	I^2(%)
Healthy Individuals	HPV-16	9	0.049	0.018–0.128	Random-effects	24.31	8	0.002	67.09
	HPV-18	11	0.034	0.020–0.056	Fixed-effects	5.50	10	0.855	0
	HPV-6	3	0.008	0.003–0.021	Fixed-effects	0.15	2	0.924	0
	HPV-11	2	0.045	0.009–0.198	Fixed-effects	1.86	1	0.172	46.44
Lesion-Bearing Patients	HPV-16	17	0.090	0.050–0.157	Random-effects	97.93	16	< 0.001	83.66
	HPV-18	19	0.076	0.050–0.115	Random-effects	47.41	18	< 0.001	62.03
	HPV-6	6	0.070	0.048–0.100	Fixed-effects	4.04	5	0.542	0.0
	HPV-11	7	0.060	0.027–0.129	Random-effects	15.90	6	0.014	62.26
	HPV-31	5	0.026	0.012–0.055	Fixed-effects	4.21	4	0.378	5.01
	HPV-33	5	0.024	0.004–0.139	Random-effects	19.78	4	0.001	79.78

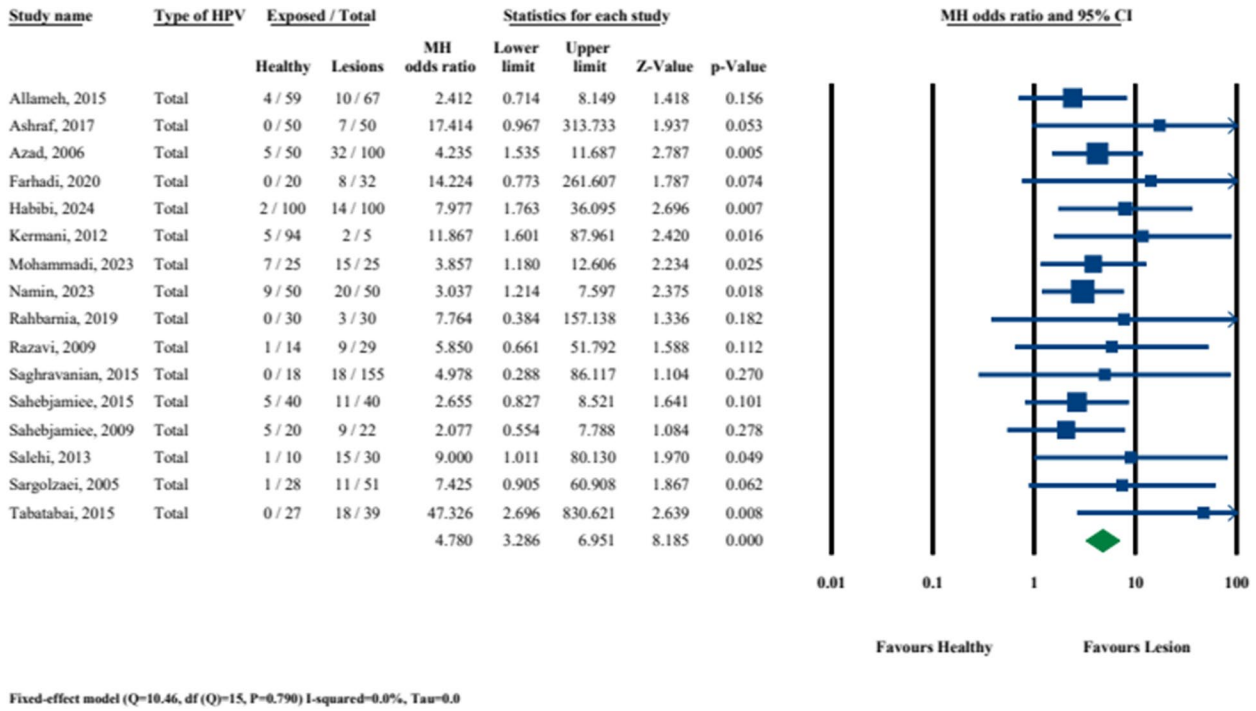

Fig. 3 Forest plot of the comparative HPV analysis conducted on case–control studies

Miller et al. [65] conducted a pioneering meta-analysis on the prevalence of oral HPV infection across normal mucosa, precancerous, and cancerous lesions. Their findings revealed that the prevalence of HPV was 10.0% in normal mucosa, 22.2% in leukoplakia, 29.5% in verrucous carcinoma, and 46.5% in OSCC. The study concluded that HPV is 2–3 times more likely to be detected in precancerous lesions and 4.7 times more likely in OSCC than in normal oral mucosa. The findings of this study regarding the prevalence of HPV in normal mucosa are nearly consistent with our findings. However, in the case of OSCC, our study reported a lower prevalence (22.7%). Melo et al., in their review, reported an even lower HPV prevalence of 4.4% in OSCC patients than in the present study; however, the association between HPV infection and OSCC could not be established because of the absence of longitudinal studies [66]. Since different histopathological grades of OSCC have distinct associations with HPV [67, 68], the variation in findings between these studies may be explained.

Mariz et al., in their global study on the prevalence of HPV-driven oropharyngeal SCC (OPSCC), reported a

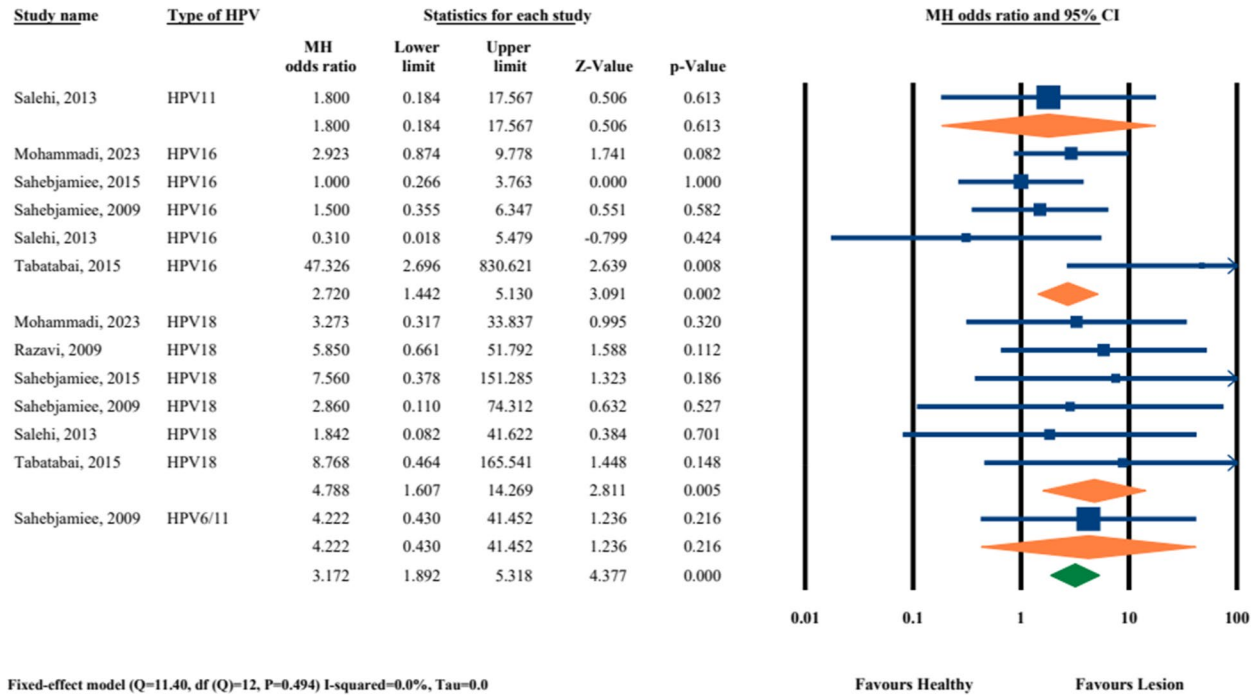

Fig. 4 Forest plot of comparative analysis with HPV subtype subgrouping

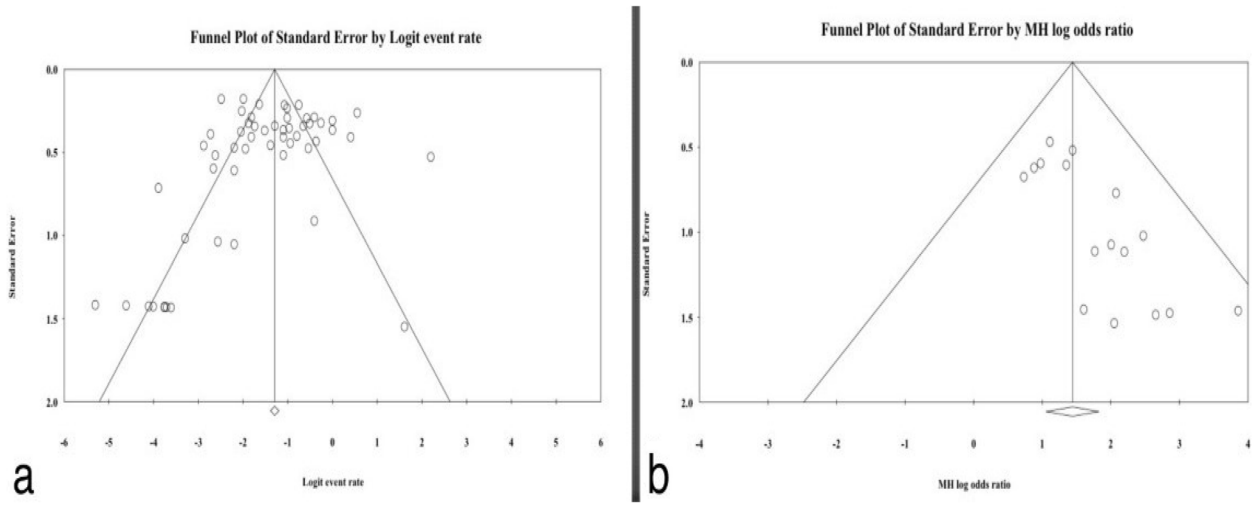

Fig. 5 Funnel plots of the overall and comparative HPV analysis; **a** Funnel plot of the overall HPV analysis. **b** Funnel plot of the comparative HPV analysis

pooled oral HPV prevalence of 44.8% in OPSCC [69]. Additionally, Abogunrin et al. assessed the prevalence of HPV in head and neck cancers among European populations and reported a pooled prevalence of 40%, with the highest rate observed in tonsillar cancer at 66.4% [70]. The disparity with our findings on oral HPV prevalence in OSCC could be attributed in part to the well-established link between HPV and oropharyngeal carcinoma, which has not been definitively proven for OSCC.

Additionally, Syrjänen et al. [71] suggested a significant link between oral HPV infection and OSCC or OPMD. Their review revealed a strong association between HPV-DNA detection and OSCC, with an OR of 3.98, and for HPV16 alone, an OR of 3.86. They also reported an association between the presence of oral HPV infection and

OPMD (OR = 3.87), with the strongest association found for OLPs, with an OR of 5.12. Syrjänen et al., in another study, reported HPV detection rates of 13% in normal oral mucosa, 25% in leukoplakia, and 33% in OSCC [72]. Compared with our study, which reported a lower pooled prevalence, these differences may result from variations in study populations or regional factors. Nevertheless, both studies underscore the role of HPV in OSCC pathogenesis. Furthermore, both Miller [65] and Syrjänen [72] reported nearly similar prevalence rates for HPV in leukoplakia patients (22.2% and 25%, respectively).

Gillison et al. [73], using a 30-s oral rinse and gargle method followed by PCR analysis, reported an overall oral HPV prevalence of 6.9% in the U.S. population, with high-risk types accounting for 3.7% and HPV-16 being the most common subtype at 1.0%. In comparison, our study reported a higher overall oral HPV prevalence of 18.3% in the Iranian population, whereas the most common subtype remained consistent. This disparity may reflect differences in study designs, population characteristics, and levels of awareness about oral HPV and its prevention. These findings may suggest the importance of improving public education and implementing preventive strategies in developing countries, such as Iran.

Colpani et al. reported an overall oral HPV prevalence of 11.89% in Brazil, which was lower than the rates reported in the cervical, penile, and anal regions, with penile HPV being the highest. These findings contrast with our study, indicating that oral HPV infection is more prevalent in Iran than in Brazil. This highlights the need for the Iranian healthcare system to develop effective strategies to control oral HPV infections. Colpani et al. reported a 4.69% prevalence of high-risk HPV types in the oral region, which aligns closely with our findings on the prevalence of HPV-16 in healthy individuals, which was 4.9%. Moreover, regarding the influence of geographic location on HPV prevalence, these findings are consistent with those of the present study [74].

Tam et al. reported an oral HPV prevalence of 7.7% in healthy individuals without lesions, with 1.4% testing positive for high-risk HPV16. They also reported that oral HPV infection has a lower prevalence and prevalence than cervicogenital HPV infection in healthy individuals [75]. Moreover, Wood et al. conducted a systematic review on oral HPV DNA in HIV-negative, cancer-free individuals, with similar findings [76]. They reported an overall oral HPV prevalence of 7.5%, including 1.6% for HPV-16, while highlighting significant variation in the incidence, prevalence, and clearance of oral HPV across different geographic regions. The findings of these two studies on the overall prevalence of HPV in healthy individuals closely align with our results. However, their reported prevalence of HPV16 was considerably lower than that in our study. This could be another concerning factor, indicating that not only is the prevalence of oral HPV in Iran above the global average, but the prevalence of high-risk subtypes is also higher than expected.

Overall, variations in oral HPV prevalence may stem from geographic location, the presence and type of lesions, and the anatomical site of the lesions [69, 70, 77].

The risk factors associated with classical, HPV-negative OPSCC also seem to apply to HPV-related OPSCC, including smoking and alcohol use. Additionally, sexual behaviors significantly contribute to the risk of HPV-positive OPSCC, likely by promoting oral transmission of the virus. It is suggested that a shift in sexual practices toward oral sex may be responsible for the increasing prevalence of this disease among younger patients. Sex is the most prominent risk factor for HPV-related OPSCC, with a considerable percentage of the disease burden occurring in men [78].

The management of precancerous lesions, malignancies, and persistent or recurrent benign lesions associated with HPV remains an unresolved problem. Current treatments primarily involve surgical interventions and the topical or intralesional use of agents that exhibit antiproliferative and cytotoxic effects on infected cells (such as podophyllotoxin, bleomycin, 5-fluorouracil, and cidofovir) or general immune system stimulation to combat HPV (including imiquimod and intralesional immunotherapy). Certain medications, such as sinecatechins and vitamin D, possess both immunostimulatory and antiproliferative characteristics [3]. Furthermore, the high prevalence of oral HPV infection identified in this study serves as a critical warning for healthcare providers. Recent research has indicated that surgical smoke may act as a transmission route for HPV infection [79, 80]. Therefore, the use of surgical face masks, particularly N95 masks, is essential to minimize the risk of HPV transmission [81].

District-based subgrouping was impeded by the unequal distribution of healthcare resources across Iran and the concentration of studies in more developed regions, such as Tehran; when considered alongside the moderate study quality and observed heterogeneity, these factors limit the generalizability of the findings. Additionally, subgroup analyses based on lesion location, histopathological grade, and age were not feasible due to insufficient data and variability in the result reporting practices of the included studies, thereby narrowing the depth of conclusions. Moreover, significant publication bias in the comparative analysis may overestimate the effect size. Furthermore, limited public awareness and cultural stigma surrounding HPV-related behaviors, especially oral sex, likely led to underreporting, particularly within the context of religious sensitivities in Iranian culture.

Future research should aim to include underrepresented regions in Iran and stratify data by age and lesion characteristics. Longitudinal studies are also needed to investigate causal relationships between HPV infection and lesion progression, particularly OSCC pathogenesis. In addition, public health actions, including promoting HPV vaccination (nonavalent vaccines), educating on transmission routes (sexual practices and surgical smoke), and standardizing protective measures (N95 masks) in dental settings, are critical for effective prevention.

Conclusions

This study highlights a higher prevalence of oral HPV infection among individuals with lesions, with its presence significantly increasing the odds of HPV detection, particularly for the HPV-18 subtype. However, HPV-16 was identified as the most common oral HPV subtype across all individuals. On the other hand, further longitudinal studies on oral HPV are needed. Considering the high prevalence of oral HPV in Iran, multidisciplinary and community-based efforts are essential to raise awareness about transmission and prevention, aiming to reduce the burden of HPV-related oral diseases.

Abbreviations

HPV	Human Papillomavirus Virus
OSCC	Oral Squamous Cell Carcinoma
OLP	Oral Lichen Planus
OPMD	Oral Potentially Malignant Disorders
PCR	Polymerase Chain Reaction
NOS	Newcastle–Ottawa Scale
HNSCC	Head and Neck Squamous Cell Carcinoma
OPSCC	Oropharyngeal Squamous Cell Carcinoma
CC	Case Control
CS	Cross Sectional
MEH	Multifocal Epithelial Hyperplasia

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12903-025-06085-0.

Additional file 1.

Additional file 2. Forest plot of the meta-analysis conducted on studies that reported the overall prevalence of oral HPV.

Acknowledgements

We would like to acknowledge the use of OpenAI's ChatGPT as a tool in revising and refining the content, for enhancing the clarity and quality of this manuscript.

Human ethics and consent to participate declarations

Not applicable.

Authors' contributions

M.K.B. contributed to the conceptualization and methodology of the study, performed data extraction, prepared figures and tables, and writing the original draft. A.M. was involved in the methodology, conducted the formal analysis and participated in reviewing the manuscript. S.A.M. provided supervision, contributed to the review and editing process, and served as the third reviewer in cases of disagreement between MKB and AM. All authors critically reviewed and approved the final manuscript.

Funding

No funding was received for this study.

Data availability

The datasets utilized in this study are available from the corresponding author upon reasonable request. Additionally, all essential published data are included within the manuscript and/or supplementary files.

Declarations

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 28 February 2025 Accepted: 30 April 2025
Published online: 09 May 2025

References

1. Quinlan JD. Human papillomavirus: screening, testing, and prevention. Am Fam Physician. 2021;104(2):152–9.
2. Soheili M, Keyvani H, Soheili M, Nasseri S. Human papilloma virus: a review study of epidemiology, carcinogenesis, diagnostic methods, and treatment of all HPV-related cancers. Med J Islam Repub Iran. 2021;35:65.
3. Mlynarczyk-Bonikowska B, Rudnicka L. HPV infections—classification, pathogenesis, and potential new therapies. Int J Mol Sci. 2024;25(14):7616.
4. Bruni L, Albero G, Rowley J, Alemany L, Arbyn M, Giuliano AR, Markowitz LE, Broutet N, Taylor M. Global and regional estimates of genital human papillomavirus prevalence among men: a systematic review and meta-analysis. Lancet Glob Health. 2023;11(9):e1345–62.
5. Forman D, de Martel C, Lacey CJ, Soerjomataram I, Lortet-Tieulent J, Bruni L, Vignat J, Ferlay J, Bray F, Plummer M. Global burden of human papillomavirus and related diseases. Vaccine. 2012;30:F12–23.
6. Doorbar J. The human Papillomavirus twilight zone–latency, immune control and subclinical infection. Tumour Virus Res. 2023;16:200268.
7. Betz SJ. HPV-related papillary lesions of the oral mucosa: a review. Head Neck Pathol. 2019;13(1):80–90.
8. Kingsley JP, Gaikwad P, Abraham P, Muthusami JC. Human papilloma virus testing in oral squamous cell carcinoma in Southern India: a case-control study. Curr Med Issues. 2021;19(1):12–8.
9. Shukla S, Mahata S, Shishodia G, Pande S, Verma G, Hedau S, Bhambhani S, Kumari A, Batra S, Basir SF, et al. Physical state & copy number of high risk human papillomavirus type 16 DNA in progression of cervical cancer. Indian J Med Res. 2014;139(4):531–43.
10. Sanders A, Slade G, Patton L. National prevalence of oral HPV infection and related risk factors in the US adult population. Oral Dis. 2012;18(5):430–41.
11. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. bmj. 2021;372:n71.
12. Bettany-Saltikov J. Learning how to undertake a systematic review: part 1. Nurs Stand. 2010;24(50):47–55 quiz 56.
13. Ga W. The Newcastle-Ottawa Scale (NOS) for assessing the quality of non-randomised studies in meta-analyses. In: 3rd symposium on systematic reviews: beyond the basics, Oxford, UK, 3–5 July 2000. 2000:2000.
14. Warnakulasuriya S. Oral potentially malignant disorders: a comprehensive review on clinical aspects and management. Oral Oncol. 2020;102:104550.
15. Efthimiou O. Practical guide to the meta-analysis of rare events. Evid Based Ment Health. 2018;21(2):72–6.

16. Nafarzadeh S, Yahyapour Y, Khazaei M, Abbasszadeh H, Sadeghi F. Detection of human papillomavirus in oral lichen planus using real time PCR. Int J Adv Biotechnol Res. 2017;8(3):2070–4.
17. Mosannen-Mozaffari P, Falaki F, Amirchaghmaghi M, Pakfetrat A, Dalirsani Z, Saghafi-Khadem S. Multifocal epithelial hyperplasia, a rare oral infection in Asia: report of twelve cases in Iran. Med Oral Patol Oral Cir Bucal. 2010;15(4):591–5.
18. Falaki F, Amir Chaghmaghi M, Pakfetrat A, Delavarian Z, Mozaffari P, Pazooki N. Detection of human papilloma virus DNA in seven cases of focal epithelial hyperplasia in Iran. J Oral Pathol Med. 2009;38(10):773–6.
19. Akhondnezhad M, Haghshenas MR, Ghasemi M, Mousavi T. The prevalence and genotyping of human papillomavirus in patients with oral tumors in health centers and clinics of Mazandaran in Iran. Virusdisease. 2018;29(3):297–302.
20. Abbas FM, Moshref M, Nadji SAR, Fard MJK, Kargahi N. Evaluation of P53 and P63 expression and their correlation with HPV virus in oral dysplastic lesions. 67–2012:56 مجله دانشکده دندانپز شکی اصفهان.
21. Allameh A, Moazeni-Roodi A, Harirchi I, Ravanshad M, Motiee-Langroudi M, Garajei A, Hamidavi A, Mesbah-Namin SA. Promoter DNA methylation and mRNA expression level of p16 gene in oral squamous cell carcinoma: correlation with clinicopathological characteristics. Pathol Oncol Res. 2019;25(4):1535–43.
22. Saber Amoli S, Hasanzadeh A, Sadeghi F, Chehrazi M, Seyedmajidi M, Zebardast A, Yahyapour Y. Prevalence of co-infection by human papillomavirus, Epstein- barr virus and Merkel cell polyomavirus in Iranian oral cavity cancer and pre-malignant lesions. Int J Mol Cell Med. 2022;11(1):64–77.
23. Arbabi-Kalati F, Nosratzehi T, Bameri Z, Rigi FM. Detection of salivary human papilloma viruses 16 and 18 (HPV) in smoker men in an Iranian population by PCR: a pilot study. Int J High Risk Behav Addict. 2014;3(3):e18053.
24. Ashraf MJ, Hosseini S, Monabati A, Valibeigi B, Khademi B, Abedi E, Azarpira N. The prevalence of human papilloma virus in squamous cell carcinoma of oral tongue. Iran J Pathol. 2017;12(2):144–9.
25. Mokhtari-Azad T, Moradi A, Khodayari-Nemin A, Reza Keikhaee M, Sargolzaei S, Shahrokhi M. Detection of human papillomavirus DNA in intraosseus ameloblastoma. Int J Virol. 2006;2(1):1–6.
26. Azmoudeh F, Aslanimehr M, Alizadeh SA, Sadeghi H, Zamanpoor S, Mokhlesi A. Molecular prevalence of human papillomavirus types 16 and 18 in oral squamous cell carcinoma using real-time PCR. Arch Razi Inst. 2024;79(2):361–6.
27. Dayyani F, Tavakolian S, Goudarzi H, Biucki FY, Faghihloo E. Prevalence of HSV, Varicella-Zoster, CMV, EBV and HPV in the oral cavity and the larynx carcinoma in Iran. Futur Virol. 2021;16(2):141–51.
28. Delavarian Z, Pakfetrat A, Falaki F, Pazouki M, Pazouki N. The role of viruses in oral squamous cell carcinoma in young patients in Khorasan (Northeast of Iran). J Appl Sci. 2010;10(11):981–5.
29. Falaki F, Dalirsani Z, Pakfetrat A, Falaki A, Saghravanian N, Nosratzehi T, Pazouki M. Clinical and histopathological analysis of oral squamous cell carcinoma of young patients in Mashhad, Iran: a retrospective study and review of literature. Med Oral Patol Oral Cir Bucal. 2011;16(4):e473–477.
30. Farhadi S, Sadri D, Bandehpour M, Akbari M, Jafarzadeh E, Hashemi M. Detection of human papillomavirus 33 in erosive oral lichen planus. Int J Cancer Manag. 2020;13(10):e101488.
31. Habibi L, Farzi R, Pirbonyeh N, Edalat F, Letafati A, Moattari A. Correlation between sampling site and prevalence of human papilloma virus (HPV) in patients with oral cancer referred to Shiraz, Iran. Oral Sci Int. 2024;21(3):1–7.
32. Haddadi M, Atefmehr L, Motlaghzadeh S, Hejami F, Elyasi FS, Zafarian N, Taghiabadi Z, Aboofazeli A, Yarahmady H, Modaresi P, et al. Prevailing of HPV-16 and 52 genotype in 2022–2023 in Sanandaj. Iran Virol J. 2024;21(1):106.
33. Haghighat S, Rezazadeh F. Prevalence of non-odontogenic infectious lesions of oral mucosa in a group of Iranian patients during 11 years: a cross sectional study. Iran J Microbiol. 2019;11(5):357–62.
34. Halimi M. Human papillomavirus infection in lung vs. oral squamous cell carcinomas: a polymerase chain reaction study. Pak J Biol Sci: PJBS. 2011;14(11):641–6.
35. Haratian K, Meybodi AM, Moradi SZ, Vosough P. Detection of high risk human papillomavirus DNA sequences in head and neck squamous cell carcinoma in Iranian Fanconi anemia patients. Yakhteh. 2010;12(1):43–50+128.
36. Jahanshahi G, Mahzooni P, Mardani H. Evaluation of correlation between human papilloma virus and P53 proteins expression in oral squamous cell carcinoma. J Dent. 2005;6(1, 2):10–17.
37. Niya MHK, Tameshkel FS, Panahi M, Salim FB, Monavari SHR, Keyvani H. Human papillomavirus investigation in head and neck squamous cell carcinoma: initial report from the low risk HPV types associations. Asian Pac J Cancer Prev: APJCP. 2017;18(9):2573.
38. Karimi A, Mohebbi E, McKay-Chopin S, Rashidian H, Hadji M, Peyghambari V, Marzban M, Naghibzadeh-Tahami A, Gholipour M, Kamangar F, et al. Human papillomavirus and risk of head and neck squamous cell carcinoma in Iran. Microbiol Spectr. 2022;10(4):e0011722.
39. Karimi A, Mohebbi E, McKay-Chopin S, Hadji M, Rashidian H, Marzban M, Naghibzadeh-Tahami A, Gholipour M, Eslami H, Kamangar F, et al. Association of opium use and tobacco smoking with α-, β-, and γ-human papillomavirus oral infection. Int J Cancer. 2024;5:1544.
40. Kermani IA, Seifi S, Dolatkhah R, Sakhinia E, Dastgiri S, Ebrahimi A, Lotfy A, Esmaeili H, Mohammadi G, Naderpour M. Human papilloma virus in head and neck squamous cell cancer. Iran J Cancer Prev. 2012;5(1):21.
41. Khalesi S, Eskandari S, Jahanshahi G, Nasr F. Human papillomavirus in oral squamous cell carcinoma using p16 and its co-relationship with cervical lymph node metastasis and clinicopathological parameters. Dent Res J (Isfahan). 2023;20:56.
42. Makvandi M, Jalilian S, Faghihloo E, Khanizadeh S, Ramezani A, Bagheri S, Mirzaei H. Prevalence of human papillomavirus and co-infection with Epstein-barr virus in oral and oropharyngeal squamous cell carcinomas. Asian Pac J Cancer Prev. 2022;23(11):3931–7.
43. Mohammadi M, Abbaszadeh H, Mohtasham N, Salehiniya H, Shafaie E. The association between high-risk human papillomavirus and oral lichen planus. Clin Exp Dent Res. 2023;9(1):93–9.
44. Moshiri F, Siadati S, Shokri-Shirvani J, Haji-Ahmadi M, Shafaei S, Yahyapour Y. Detection of HPV infection in non-cancer oesophageal lesions and normal tissue by nested polymerase chain reaction. West Indian Med J. 2016;65(3):496–9.
45. Moshref M, Mehrdad L, Jadali F, Mashhadi AF, Kharazifard M, Shamshiri A. Correlation between P53, P63 expression and HPV infection with staging and grading of oral squamous cell carcinoma. 2010.
46. Namin AK, Azad TM, Eslami B, Sarkarat F, Shahrokhi M, Kashanian F. A study of the relationship between ameloblastoma and human papilloma virus. J Oral Maxillofac Surg. 2003;61(4):467–70.
47. Nikakhlagh S, Saki N, Shoar MH, Sartipipor A, Saki S. Incidence of etiologic factors in squamous cell carcinoma of head and neck in ahvaz. Iran J Otorhinolaryngol. 2012;24(67):85–90.
48. Nili A, Daneshpazhooh M, Mahmoudi H, Kamyab K, Jamshidi ST, Soleiman-Meigooni S, Darvishi M. Tracing human papillomavirus in skin and mucosal squamous cell carcinoma: a histopathological retrospective survey. Dermatol Rep. 2024;16(2):9833.
49. Pouide E, Arefian E, Deldar AA. Evaluation of Human Papilloma Virus (HPV) genotypes diversity in oral cancer lesions of patients in Imam Khomeini Hospital. Pathobiol Res. 2016;19(2):19–27.
50. Rahbarnia L, Farajnia S, Bayazian G, Naderpour M, Feizi H. Prevalence of human papillomavirus in patients with oral squamous cell carcinoma in Tabriz, Iran. 2019.
51. Razavi Nikoo H, Ardebili A, Ravanshad M, Rezaei F, Teimoori A, Khanizadeh S, Pouriayevali MH, Ajorloo M. E6-specific detection and typing of human papillomaviruses in oral cavity specimens from Iranian patients. Iran Biomed J. 2017;21(6):411–6.
52. Razavi SM, Ghalayani P, Salehi MR, Attarzadeh H, Shahmoradi M. Human papilloma virus as a possible factor in the pathogenesis of oral lichen planus. Dent Res J. 2009;6(2):82.
53. Rezaei M, Karimi Galougahi M, Kheradmand A, Pourabdollah Toutkaboni M. Mir Mohammad Sadeghi H, Abdollahi A, Emami Razavi A, Safavi Naini A, Bidari-Zerehpoosh F: The frequency of human papillomavirus positivity in Iranian patients with head and neck squamous cell carcinoma. Iran J Pathol. 2021;16(1):20–6.
54. Saghravanian N, Ghazi N, Meshkat Z, Mohtasham N. Human papillomavirus in oral leukoplakia, verrucous carcinoma, squamous cell carcinoma, and normal mucous membrane. Oman Med J. 2015;30(6):455–60.

55. SahebJamee M, Boorghani M, Ghaffari S-R, AtarbashiMoghadam F, Keyhani A. Human papillomavirus in saliva of patients with oral squamous cell carcinoma. Med Oral Patol Oral Cirugia Bucal. 2009;14(10):E525–8.
56. Sahebjamiee M, Sand L, Karimi S, Biettolahi JM, Jabalameli F, Jalouli J. Prevalence of human papillomavirus in oral lichen planus in an Iranian cohort. J Oral Maxillofac Pathol. 2015;19(2):170–4.
57. Salehi M, Khozeimeh F, Razavi S, Kia S, Ghorbani S. Comparison of human papilloma virus genotypes in patient with leukoplakia and mild dysplasia and health persons by polymerase chain reaction. 2013.
58. Soodabe S, Mohammadreza K, Abdolvahhab M, Mohammedreza G, Hossein N. Detection of Human Papilloma Virus DNA Genotypes in oral squamous cell carcinoma. 2005.
59. Seifi S, Asvadi Kerman I, Dolatkhah R, Asvadi Kermani A, Sakhinia E, Asgarzadeh M, Dastgiri S, Ebrahimi A, Asghari Haggi A, Nadri M, Asvadi Kerman T. Prevalence of oral human papilloma virus in healthy individuals in East Azerbaijan Province of Iran. Iran J Public Health. 2013;42(1):79–85.
60. Seraj JM, Yazdani N, Ashtiani ZO, Seraj SM, Hasheminasab SM, Memar B, Mirashrafi F, Borghei H, Yazdani J, Mostaan LV. TP53 gene expression in HPV-positive oral tongue SCC and its correlation with nodal metastasis. Pathol Res Pract. 2011;207(12):758–61.
61. Tabatabai SH, Nabieyan M, Sheikhha MH, Zarmehi S, Tadbir AA, Ahmadi NA. Detection of Human papillomavirus 16 and 18 types in oral squamous cell carcinoma patients in Yazd, Iran: a case-control study. Arch Adv Biosci. 2015;6(1):11–7.
62. Yahyapour Y, Shamsi-Shahrabadi M, Mahmoudi M, Motevallian A, Siadati S, Shefaii S, Shirvani JS, Mollaie HR, Monavari SH, Keyvani H. High-risk and low-risk human papillomavirus in esophageal squamous cell carcinoma at Mazandaran, Northern Iran. Pathol Oncol Res. 2013;19(3):385–91.
63. Zareei M, Moradi A, Chamani G, Kakouei S, Hamkar R, Mohammad AS, Alizadeh N, Eslami B. Detection of human papillomavirus DNA sequences in oral lesions using polymerase chain reaction. 2007.
64. Zargaran M, Azizi Jalilian F. Prevalence and risk factors of oral HPV infection among a healthy Iranian population; Kurdistan. West of Iran J Med Virol. 2020;92(12):3821–9.
65. Miller CS, Johnstone BM. Human papillomavirus as a risk factor for oral squamous cell carcinoma: a meta-analysis, 1982–1997. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2001;91(6):622–35.
66. Melo BAC, Vilar LG, Oliveira NR, Lima PO, Pinheiro MB, Domingueti CP, Pereira MC. Human papillomavirus infection and oral squamous cell carcinoma - a systematic review. Braz J Otorhinolaryngol. 2021;87(3):346–52.
67. Chua BQY, Chong VWS, Kadir HBA, Yeo BSY, Fong PY, Jang IJH, Lim CM. Histopathological prognostic factors of surgically treated HPV-associated oropharyngeal squamous cell carcinoma: a systematic review and meta-analysis. Ann Surg Oncol. 2024;32:1280–300.
68. Fujimaki M, Fukumura Y, Mitani K, Kurisaki A, Yokoyama J, Ikeda K, Yao T. Histological subtypes and characteristic structures of HPV-associated oropharyngeal carcinoma; study with Japanese cases. Diagn Pathol. 2013;8(1):211.
69. Mariz BALA, Kowalski LP, William WN Jr, de Castro JG, Chaves ALF, Santos M, de Oliveira TB, Araújo ALD, Normando AGC, Ribeiro ACP. Global prevalence of human papillomavirus-driven oropharyngeal squamous cell carcinoma following the ASCO guidelines: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2020;156:103116.
70. Abogunrin S, Di Tanna GL, Keeping S, Carroll S, Iheanacho I. Prevalence of human papillomavirus in head and neck cancers in European populations: a meta-analysis. BMC Cancer. 2014;14:1–13.
71. Syrjänen S, Lodi G, von Bültzingslöwen I, Aliko A, Arduino P, Campisi G, Challacombe S, Ficarra G, Flaitz C, Zhou HM, et al. Human papillomaviruses in oral carcinoma and oral potentially malignant disorders: a systematic review. Oral Dis. 2011;17(Suppl 1):58–72.
72. Syrjänen KJ, Syrjänen S. Papillomavirus infections in human pathology. (No Title) 2000.
73. Gillison ML, Broutian T, Pickard RK. Tong Z-y, Xiao W, Kahle L, Graubard BI, Chaturvedi AK: Prevalence of oral HPV infection in the United States, 2009–2010. JAMA. 2012;307(7):693–703.
74. Colpani V, Soares Falcetta F, Bacelo Bidinotto A, Kops NL, Falavigna M, Serpa Hammes L, Schwartz Benzaken A, Kalume Maranhão AG, Domingues C, Wendland EM. Prevalence of human papillomavirus (HPV) in Brazil: a systematic review and meta-analysis. PLoS ONE. 2020;15(2):e0229154.
75. Tam S, Fu S, Xu L, Krause KJ, Lairson DR, Miao H, Sturgis EM, Dahlstrom KR. The epidemiology of oral human papillomavirus infection in healthy populations: a systematic review and meta-analysis. Oral Oncol. 2018;82:91–9.
76. Wood ZC, Bain CJ, Smith DD, Whiteman DC, Antonsson A. Oral human papillomavirus infection incidence and clearance: a systematic review of the literature. J Gen Virol. 2017;98(4):519–26.
77. Aghaeipour F, Salehiniya H, Abbaszadeh H. Prevalence of human papillomavirus (HPV) in oral mucosal lesions in Iran: a systematic review and meta-analysis. J Med Virol. 2021;93(11):6089–99.
78. Whitton AF, Knight GL, Marsh EK. Risk factors associated with oral Human Papillomavirus (HPV) prevalence within a young adult population. BMC Public Health. 2024;24(1):1485.
79. Hu X, Zhou Q, Yu J, Wang J, Tu Q, Zhu X. Prevalence of HPV infections in surgical smoke exposed gynecologists. Int Arch Occup Environ Health. 2021;94:107–15.
80. Imani B, Merajikhah A, Khazaei S, Bouraghi H. Surgical smoke and transmission of coronavirus to surgical team members; a letter to editor. Surg Innov. 2020;28(5):654–5.
81. Palma S, Gnambs T, Crevenna R, Jordakieva G. Airborne human papillomavirus (HPV) transmission risk during ablation procedures: a systematic review and meta-analysis. Environ Res. 2021;192:110437.

Publisher's Note