

# Knowledge about the relation between human papillomavirus and oropharynx squamous cell carcinomas among university students : a systematic review and meta-analysis

## ABSTRACT

**Background:**The human papillomavirus (HPV) is the most common sexually transmitted infection globally and is linked to certain types of cancer, including oropharynx squamous cell carcinomas (OPSCC). Unfortunately, a large part of the population is unaware of this connection. University students play a crucial role in spreading scientific knowledge, and many studies have been conducted to assess their knowledge on the subject. However, no study has collated data from previous research. Therefore, our study aims to carry out a systematic review with meta-analysis to determine the level of knowledge among university students regarding the link between HPV and OPSCC. **Methodology:**We conducted a systematic review according to the recommendations of the preferred reporting items for systematic reviews and meta-analyses (PRISMA). We include 22 of a total of 290 studies. **Results:**The overall pooled prevalence of university students who knew the relation between HPV and OPSCC was 45.00% (95% CI: 35.00-55.00). According to the subgroup meta-analysis, the pooled prevalence was highest in dental students 64.00% (95% CI: 47.00-79.00), followed by medical students 39.00% (95% CI: 18.00-66.00), and the lower prevalence was the health student group 35.00% (95% CI: 27.00-43.00). **Conclusion:**This systematic review revealed low knowledge about the relationship between HPV and OPSCC among university students, but better knowledge among dental students.

*Keywords:* HPV, university students, oropharyngeal cancer

## 1. INTRODUCTION

Sexually transmitted infections are a major global health issue. The human papillomavirus (HPV) is the most common sexually transmitted infection worldwide and can be transmitted through sexual contact, including oral sex [1].

Aside from the well-known risks associated with alcohol and smoking, HPV is also responsible for a significant proportion of oropharynx squamous cell carcinomas (OPSCC).

In developed countries, HPV-related OPSCC has become the most common type of oropharyngeal cancer [2-5]. In the US and UK, HPV is responsible for 71% and 51.8% of all OPSCC cases, respectively [6]. The majority of these cases (85-96%) are caused by HPV-16 infections, which can be prevented by HPV vaccination [7-8]. However, the percentage of HPV-related OPSCC varies depending on geographical region, the decade of study, and population sexual behaviour [9].

Although HPV is associated with several types of cancer, many people are unaware of its link to non-gynecological cancers, such as OPSCC. This is concerning because most awareness campaigns focus solely on the prevention of cervical cancer.

In this context, it is important to investigate the level of awareness university students have of HPV-associated cancers, as they play a crucial role in disseminating scientific knowledge.

Fewer studies were published concerning the knowledge of OPSCC HPV-related cancers by university students. Osazuwa-Peters and Tutlam (2016) studied 100 university students from non-health-related courses, 81% had low awareness of oral cavity and oropharyngeal cancer, and only 2% perceived that the risk of cancer of the oral cavity and oropharynx was high [10]. In another study, Alzabibi et al. (2022) revealed a gap in knowledge among students about the anatomical sites for cancers of the mouth, as only 27.5% of the participants knew that the floor of the mouth and the tongue are the most common sites for oral cancer [11].

Another study carried out in Poland studied a total of 1710 university students, they were divided in two groups of medical and non-medical students. Only 59.38% of non-medical students had heard about HPV, while only 44.74% knew about the HPV vaccine. Only 55.92% of non-medical students knew about the oncogenic potential of HPV, compared to 81.17% of medical students. Furthermore, about half of the respondents in both groups did not know about the risk of developing oral or oropharyngeal cancer [12].

On the other hand, some studies showed adequate knowledge by university students regarding HPV. The study by Keser et al. (2021) [13] and the study conducted by Tarakji (2022) [14] showed that 83 and 78% respectively of the students knew the relationship between HPV and oropharyngeal cancer.

Thus, it is necessary to know what is the real level of knowledge about the relationship between HPV and oropharyngeal cancer among university students and whether there is a difference in knowledge among students from different university courses. The present study aimed to perform a systematic review and meta-analysis of knowledge about the relationship between human papillomavirus (HPV) and OPSCC among university students.

## 2. MATERIAL AND METHODS

### 2.1 Searching strategies

We conducted a systematic review and meta-analysis according to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [15]. We searched published literature in MEDLINE/PubMed, The Cochrane Central Register of Controlled Trials (CENTRAL), LILACS, EMBASE, SCOPUS and Gray literature for articles published up to February 2023.

The following keywords were used to search in the titles and abstracts: ("HPV" OR "papillomavirus" OR "papillomaviridae") AND (("head" AND "neck") OR "oropharynx" OR "oropharyngeal" OR "tongue" OR "mouth" OR "oral" OR "oral cavity") AND ("cancer" OR "tumor" OR "neoplasms" OR ("carcinoma" AND "squamous" AND "cell")) AND ("knowledge" OR "Awareness" OR "Know" OR "Known" OR "understand") AND "students".

### 2.2 Inclusion and exclusion criteria

We searched for articles reporting the impact of knowledge regarding HPV and its relation to OPSCC among university students. We include articles in English, Portuguese or Spanish. Any type of study design was considered and no restriction on the publication date of the article.

We exclude review articles, meta-analyses, case reports, animal studies and articles with incomplete information.

### 2.3 Selection of studies

Two researchers CDBS and FJBLF independently screened titles and abstracts for eligibility in the period from January to February 2023. Any discrepancies between all investigators were resolved by

the third investigator (CCF). A PRISMA workflow diagram was created to show how the studies were included (Fig 1.)

## 2.4 Data extraction

Two investigators (CDBS and FJBLF) independently extracted the data from the selected studies and data were reviewed by a third investigator. We use a form to extract the following data from each study: author name, publication year, country, study design, sample size, graduation, aims, methods, knowledge about the relation between HPV and OPSCC, findings and conclusions.

## 2.5 Statistical analysis

All the statistical analyses for the meta-analysis were developed in R software (version 4.2.2 and package meta version 6.2-0).  $I^2$  statistics were applied for the evaluation of study heterogeneity, where 25, 50, and 75% represented low, moderate, and severe heterogeneity, respectively. A random-effect model was employed to conduct the meta-analysis because of high heterogeneity. We use the random effect model, with a 95% confidence interval to estimate the pooled prevalence because of the high heterogeneity of the included studies (99%) [16].

We analyzed the prevalence of students who knew the relationship between HPV and oropharyngeal cancer. As the studies were heterogeneous, with students from different courses, we divided them into three groups: medical students, health students and dental students.

## 2.6 Quality assessment

The quality of the studies included in this systematic review was evaluated following the checklist proposed by the Joanna Briggs Institute Critical Appraisal Checklist for Studies Reporting Prevalence Data [17]. The checklist contains nine questions with four answering options including Yes, No, Unclear and Not applicable; studies were characterized as follows: low risk of bias (> or = 70% of questions answered "yes"), moderate risk of bias (> or = 50% and 70% of questions answered "yes" and high risk of bias (50% of questions answered "yes"). In our review, 21 studies were considered as presenting low risk and 1 as moderate risk of bias as shown in Table 2.

# 3. RESULTS

## 3.1 Search results

A total of 289 studies were retrieved with our search strategy, in addition, we included 1 article manually. After removing duplicate articles, 170 studies remained. Reading the titles and abstracts of these studies, 46 studies were eligible to read the full article. After reading the full text of the selected articles, we excluded 22 articles for reasons such as no access to full text (n=11) and literature reviews, systematic reviews, case studies, and conference proceedings (n=12). There were 22 studies left that were included in this systematic review. Fig 1. shows the flow of studies throughout the review. A summary of study characteristics is presented in Table 1. Included studies evaluated 11,362 participants from 22 studies that provided data for quantitative analysis.

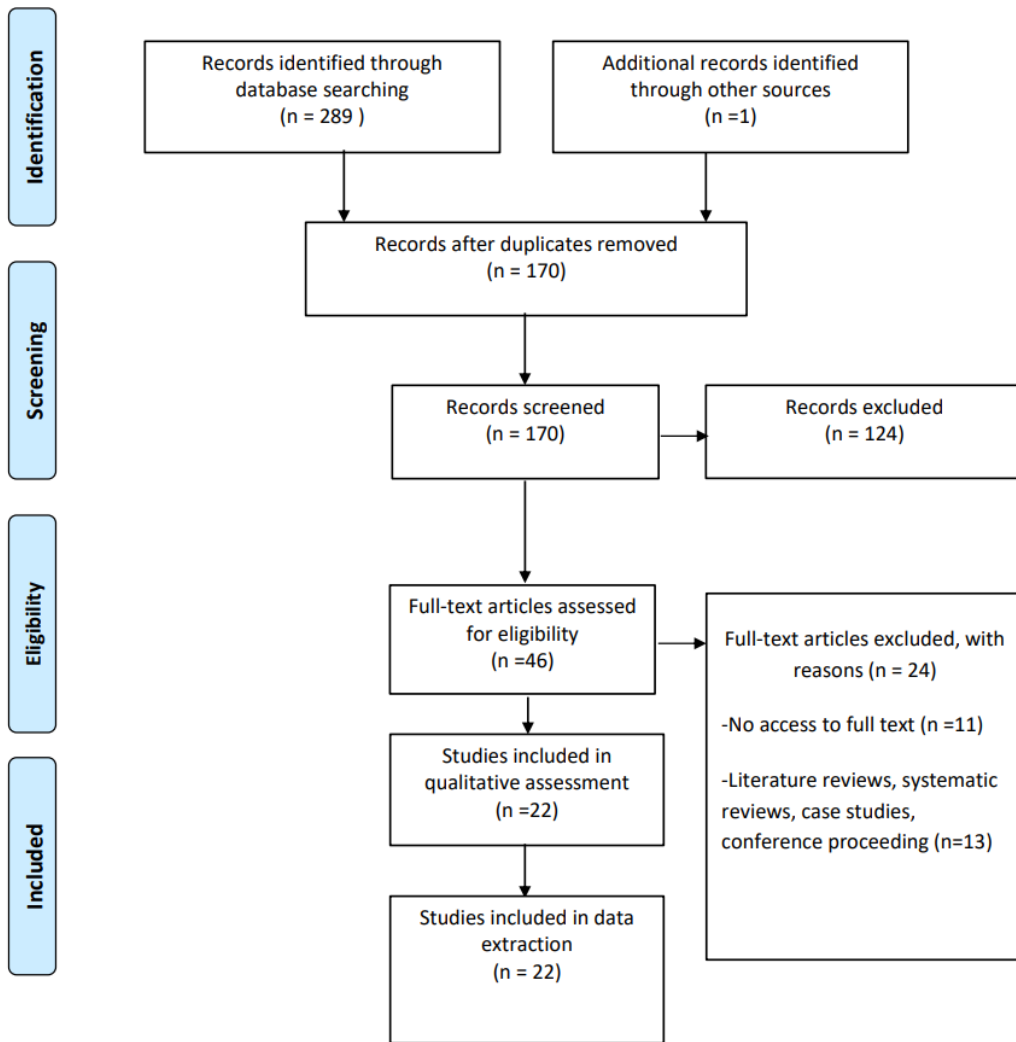


Fig. 1 PRISMA diagram of study identification and screening.

**Table 1** Published studies included

Authors/ year	Country	Study design	Graduation	Total Students	Students that knew n (%)*
Alzabibi et al. (2022)	Syria	Cross-sectional study	Medical	301	148 (49.1 %)
Balaji et al. (2020)	India	Cross-sectional study	Medical and Dental	577	308(53.37 %)
Biselli- Monteiro et al. (2020)	Brazil	Cohort study	Health courses	492	94(19,11 %)
Dodd et al. (2021)	UK	Cross-sectional study	Health courses	1415	354 (25 %)
Du et al. (2022)	UK	Cross-sectional study	Medical	247	53(21.5 %)
Evans et al. (2019)	USA	Cross-sectional study	Medical and public health	333	112 (33.63 %)
Ferreira et al. (2023)	Brazil	Cross-sectional study	Medical and Nursing	201	95(47.26%)
Jeruzal- Świątecka et al., 2020	Poland	Cross-sectional study	Medical and others	1710	750(43.86%)
Kavanagh et al. (2020)	Ireland	Cross-sectional study	Several	1494	239 (16%)
Keser et al. (2020)	Peru	Cross-sectional study	Dental	318	263(82.7%)
Lewandowski et al. (2018)	Polonia	Cross-sectional study	Several	196	79 (40.31% )
Lingam et al. (2022)	Various	Cross-sectional study	Dental	886	686 (77.43%)
Lorenzo- Pouso et al. (2018)	Holand	Cross-sectional study	Dental	158	114(72.15%)
McCready et al. (2014)	USA	Across-sectional study	Medical and others	85	47 (55.29%)
Mlinar et al. (2022)	Slovenia	Across-sectional study	Nursing	175	55 (31.43%)

Poelman et al. (2017)	Holand	Across-sectional study	Dental	196	80 (40.82%)
Rutkoski et al. (2019).	USA	Across-sectional study	Dental	380	304 (80%)
Sallam et al. (2019)	Jordan	Across-sectional study	Dental	376	249 (66.22%)
Sallam et al. (2021)	Jordan	Across-sectional study	Medical	1198	199 (16.61)
Saranya et al. (2017)	India	Across-sectional study	Dental	100	20 (20%)
Tarakji et al. (2021)	Saudi Arabia	Across-sectional study	Medical	189	147 (77.78%)
Vieira et al. (2022)	Brazil	Across-sectional study	Several	335	103 (30.75%)

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\* N° of students that Knew about the relation between HPV and OSCC

### 3.2 Characteristics of included studies

22 studies with 11.362 participants were included in this systematic review. These studies were conducted in different countries [11-14, 18-36]. As depicted in Table 1, a total of 21 cross-sectional studies and 1 Cohort study, were included.

Regarding the sample size of included studies, 85 is the smallest number of participants and 1710 is the maximum number of participants.

### 3.3 Quality of included studies

The quality of the papers included in this systematic review was evaluated following the checklist proposed by the Joanna Brigs Institute Critical Appraisal Checklist for Studies Reporting Prevalence Data [15]. In our systematic review, 21 studies were considered as presenting low risk and 1 presenting moderate risk of bias, as shown in Table 2.

### **3.4 Meta-analysis of the prevalence of knowledge about the relationship between HPV and OPSCC among university students**

In our study, the percentage of students that knew about the relationship between human papillomavirus (HPV) and oropharyngeal cancer among university students range from 16.00% to 82.70%. The pooled amount of students that know the relation between human papillomavirus (HPV) and oropharyngeal cancer in this study was 45% (95% CI, 35% - 55%) among university students.

The Fig 2. shows the forest plot illustrating the individual prevalence of each study and the pooled prevalence of this systematic review and meta-analysis.

The studies had high heterogeneity ( $I^2 = 99\%$ ). The overall pooled prevalence of university students that know the relation between HPV and oropharyngeal cancer was 45.00% (95% CI: 35.00-55.00). When we analyzed and separated the studies with just dental students the pooled prevalence of students that knew the relation between the HPV and the oropharyngeal cancer was 66% (95% CI, 50% - 79%). The Fig 2. shows the forest plot illustrating the individual prevalence of studies with dental students.

### **3.5 Subgroup Meta-analysis**

According to the subgroup meta-analysis the pooled prevalence was highest in dental students 64.00% (95% CI: 47.00-79.00), followed by medical students 39.00% (95% CI: 18.00-66.00). And the lower prevalence was the health student group 35.00% (95% CI: 27.00-43.00).

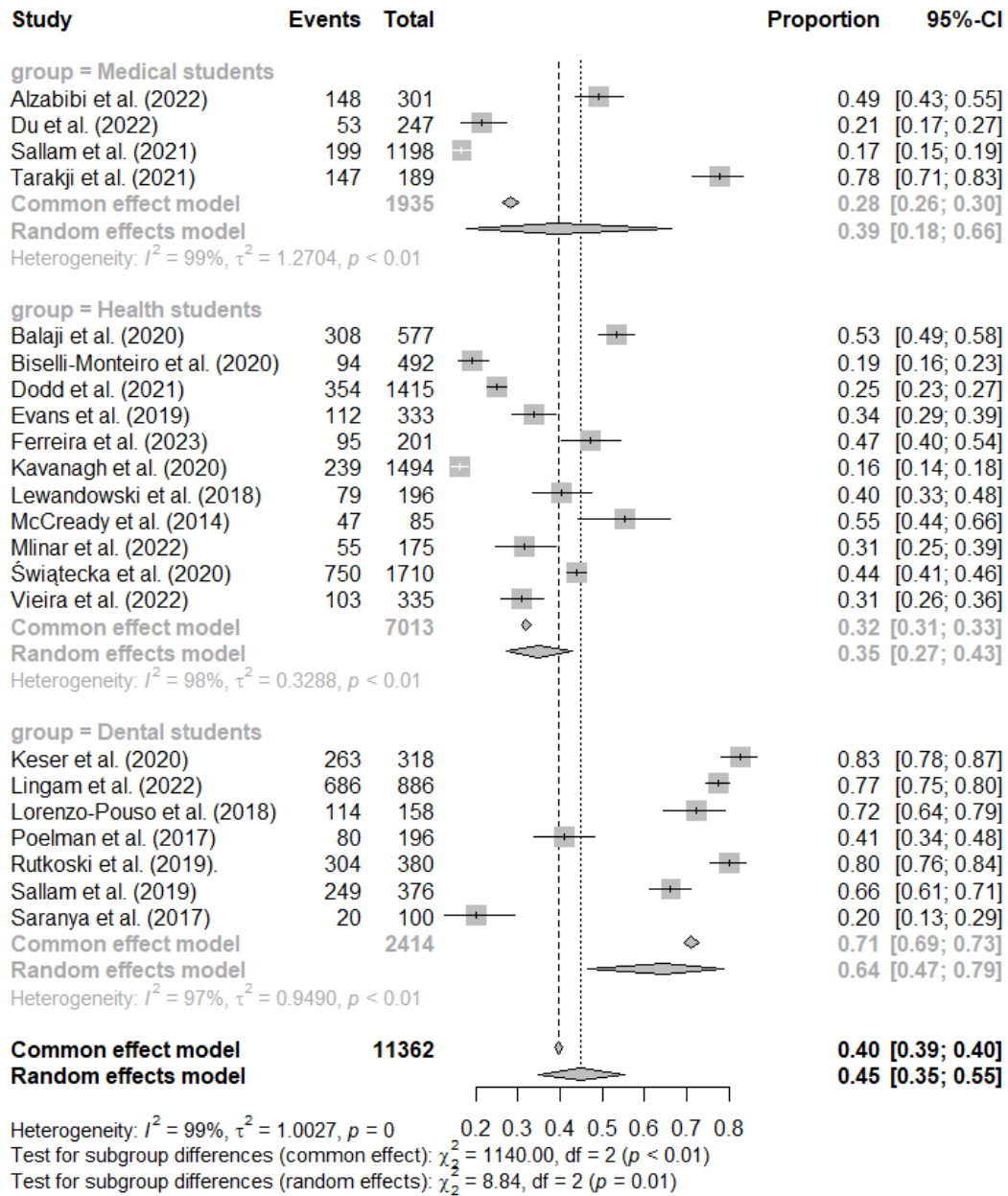


Fig. 2 Forest plot of a meta-analysis of studies reporting level of knowledge about HPV and OPSCC among university students.

**Table 2** Risk of bias assessment according to the Joanna Briggs Institute critical appraisal tool for prevalence studies

Authors/year	Q 1	Q 2	Q 3	Q 4	Q 5	Q 6	Q 7	Q8	Q 9	Total (%of "yes")	Risk of bias
Alzabibi et al. (2022)	Y	Y	Y	Y	Y	Y	Y	Y	Y	100	Low
Balaji et al. (2020)	Y	Y	Y	Y	Y	Y	Y	Y	Y	100	Low
Biselli-Monteiro et al. (2020)	Y	Y	Y	Y	Y	Y	Y	Y	Y	100	Low
Dodd et al. (2021)	Y	Y	Y	Y	Y	Y	Y	Y	Y	100	Low
Du et al. (2022)	Y	Y	Y	Y	Y	Y	Y	Y	Y	100	Low
Evans et al. (2019)	Y	Y	Y	Y	Y	Y	Y	Y	Y	100	Low
Ferreira et al. (2023)	Y	Y	Y	Y	Y	Y	Y	Y	Y	100	Low
Jeruzal-Świątecka et al., 2020	Y	Y	Y	N	Y	Y	Y	Y	Y	88.89	Low
Kavanagh et al. (2020)	Y	Y	Y	Y	Y	Y	Y	Y	Y	100	Low
Keser et al. (2020)	Y	Y	Y	Y	Y	Y	Y	Y	Y	100	Low
Lewandowski et al. (2018)	Y	Y	Y	Y	Y	Y	Y	Y	Y	100	Low
Lingam et al. (2022)	N	Y	Y	Y	Y	Y	Y	Y	Y	88.89	Low
Lorenzo-Pouso et al. (2018)	Y	Y	Y	Y	Y	Y	Y	Y	Y	100	Low
McCready et al. (2014)	N	Y	N	N	Y	Y	Y	Y	Y	66.69	Moderate
Mlinar et al. (2022)	Y	Y	Y	Y	Y	Y	Y	Y	Y	100	Low
Poelman et al. (2017)	Y	Y	Y	Y	Y	Y	Y	Y	Y	100	Low

Rutkoski et al. (2019).	Y	Y	N	Y	Y	Y	Y	Y	Y	100	Low
Sallam et al. (2019)	Y	Y	Y	Y	Y	Y	Y	Y	Y	100	Low
Sallam et al. (2021)	Y	Y	Y	Y	Y	Y	Y	Y	Y	100	Low
Saranya et al. (2017)	Y	Y	Y	Y	Y	Y	Y	Y	Y	100	Low
Tarakji et al. (2021)	Y	Y	Y	Y	Y	Y	Y	Y	Y	100	Low
Vieira et al. (2022)	Y	Y	Y	Y	Y	Y	Y	Y	Y	100	Low

Note 1: Q1 = Was the sample frame appropriate to address the target population? - Q2 = Were study participants sampled in an appropriate way? - Q3 = Was the sample size adequate? - Q4 = Were the study subjects and the setting described in detail? - Q5 = Was the data analysis conducted with sufficient coverage of the identified sample? - Q6= Were valid methods used for the identification of the condition? - Q7 = Was the condition measured in a standard, reliable way for all participants? - Q8 = Was there appropriate statistical analysis? - Q9 = Was the response rate adequate, and if not, was the low response rate managed appropriately? Note 2: Y = yes; N = no; U = Unclear; NA = not applicable

#### 4. DISCUSSION

HPV is a significant risk factor for OPSCC, particularly among young individuals. Much of the population is unaware that HPV can cause this type of cancer. As university students play an important role in disseminating scientific knowledge, thus it is necessary to understand these students' level of knowledge about HPV. To better understand this issue, we performed a systematic review with meta-analysis to explore the level of knowledge about the relationship between HPV and OPSCC among college students. Our review included 24 studies with 11,362 students.

Our systematic review followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) protocol and we used the R Studio for the statistics analysis [14].

The primary outcome of interest was the level of knowledge about the association between HPV and oropharyngeal cancer. The pooled analysis of all included studies indicated that among university students, the knowledge level about this relationship ranged from 17.00% to 83.00%, with an overall pooled prevalence of 45.00% (95% CI: 35.00-55.00). This result is similar to the findings by Alzabibi et al. (2022), Ferreira et al. (2023), Levvandowsk et al. (2018), Poelman et al. (2017) and the study conducted by Jeruzal-Świątecka and Pietruszewska (2020) [11, 23, 25, 30, 12]. This suggests that while there is some awareness of the link between HPV and oropharyngeal cancer among university

students, there is also significant room for improvement in knowledge dissemination and education in this regard.

In contrast, the studies of Biselli-Monteiro et al. (2020), Dodd et al. (2021), Du et al. (2022), Kavanagh et al. (2020), Sallam et al. (2019) and Saranya et al. (2017) found 19,25,21,16,17,17 and 20% respectively [19-21, 24, 32, 34]. A possible explanation for this might be due to the heterogeneity of the studies, as we observed the different studies included students from medical, dental and other university students. So different students have different knowledge in relation to HPV and OPSCC.

Subgroup meta-analysis by type of student graduation revealed the pooled prevalence of knowledge about the association between HPV and OPSCC was highest in the dental student's group 64.00% (95% CI: 47.00-79.00), followed by medical students 39.00% (95% CI: 18.00-66.00). The lowest prevalence was found in the health student group 35.00% (95% CI: 27.00-43.00).

A particularly interesting finding in the study was the analysis of knowledge levels among dental students specifically. Dental students are likely to be more exposed to information about oral health and associated conditions, including oropharyngeal cancer. Therefore, it was expected that their knowledge about the link between HPV and oropharyngeal cancer would be higher compared to the general university student population. The results supported this hypothesis, as the pooled prevalence of knowledge among dental students was 66% (95% CI, 50% - 79%). All studies with just dental students included in this review collaborated with these findings. The exception of the study of Saranya and the study of Poelman revealed 20 and 41 % respectively. This suggests that dental education may have a positive impact on raising awareness of the HPV-cancer association, but there is still scope for further improvement.

This study has some limitations. One of the main drawbacks of conducting research studies is the potential for publication bias. This occurs when studies with positive or statistically significant outcomes are more likely to be published, which can lead to an overestimation of the overall prevalence of the phenomenon being studied. Moreover, the differences in study designs, sample sizes, and locations can introduce heterogeneity, making it difficult to draw conclusive results.

It is important to acknowledge that there are limitations in the present findings, and therefore, future research should aim to conduct larger and more standardized studies to confirm and refine the results. Additionally, it would be valuable to explore potential factors that contribute to variations in knowledge levels among different university student populations, as this could aid in developing tailored educational strategies.

## 5. CONCLUSIONS

Increasing knowledge about the relationship between HPV and oropharyngeal cancer among university students is essential to reduce the incidence of this type of cancer. By addressing the knowledge gap, promoting prevention strategies like HPV vaccination, and providing comprehensive sexual health education, universities can play a vital role in raising awareness and empowering students to take control of their health.

The results of this study show a low knowledge of medical students about HPV as a cause of OPSCC and comparatively a better knowledge of this relationship among dental students. We suggest that collaborative efforts among educational institutions, healthcare professionals, and public health organizations are needed to ensure that college students are equipped with the knowledge and resources to effectively prevent HPV-related oropharyngeal cancer.

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