

The Prevalence of Oral Cancer in Saudi Arabia – A Systematic Review

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Abstract

Background: Oral cancer is the 10th most common cancer in the world and third most common cancer in Saudi Arabia. **Objectives:** The present systematic review is conducted to assess the prevalence and causative factors of oral cancer in Saudi Arabia. **Materials and Methods:** This review conducted in adherence to PRISMA standards of quality for reporting systematic reviews and meta-analyses and was registered in PROSPERO with registration number CRD42017057791. Our systematic search included MEDLINE, EMBASE, CINAHL, PsychINFO, Scopus, and key journals and review articles; the date of the last search was December 2018. We graded the methodological quality of the studies by means of the Quality Assessment Tool for Quantitative Studies, developed for the Effective Public Health Practice Project (EPHPP). **Results:** A total of 82 studies were identified for screening, and 9 studies were eligible. All the studies were retrospective hospital records based. Oral cancer prevalence varied from 21.6% to 68.6%. Male to female ratio varied from 36.6% to 65.4%. Use of smokeless form of tobacco, Shamma was the main cause for oral cancer. **Conclusions:** The present review showed a very high prevalence of oral cancer in Saudi Arabia with the main causative agent the use of smokeless tobacco Shamma.

Keywords: Systematic review; Oral cancer; Saudi Arabia; Prevalence

Introduction

Oral cancer (OC) refers to malignancies in the mucosal lip, tongue and oral cavity associated with alcohol consumption, exposure to tobacco or both and rarely by traumatic irritation of chronic nature and exposure to human papillomavirus (HPV).

[1] Globally, OC is reported to be the tenth most commonly diagnosed cancer with an annual incidence of >300,000 cases. Incidence and mortality of OC are higher in developing countries when compared with developed countries is due to the combined effect of the aging of populations, and the high or increasing levels of prevalence of cancer risk factors. [1] In Kingdom of Saudi Arabia (KSA) lymphoma and leukemia are most common malignancies and oral cancer stands in 3rd position. [2] Among all the head and neck cancers detected yearly in KSA, oral cancer accounts for as much as 26 percent, a majority of them in advanced stage receiving palliative treatment. The frequent use of smokeless tobacco (Shammah and Quat) is considered a strong attribute in the high prevalence of oral cancer in KSA. Several authors [2-13] have documented that the high frequency of oral cancer predominantly in Jazan province and other areas of the southwestern region of the KSA is invariably related to consumption of Shammah. No previous publication has systematically reviewed the existing literature to summarize the prevalence of oral cancer in KSA. The present systematic review is conducted to assess the prevalence and causative factors of oral cancer in KSA.

Materials and Methods

This review was planned, conducted, and reported in adherence

to PRISMA standards of quality for reporting systematic reviews and meta-analyses. [14] The present review was registered in PROSPERO with registration number CRD42017057791.

Study eligibility

We included studies published in English language only that investigated the prevalence of oral cancer in KSA. Papers were excluded at this stage if they were an editorial letter, case report, *in vitro*, not investigating the prevalence of OC in KSA.

Study identification

Various research database were searched which include, MEDLINE, CINAHL, EMBASE, Educational Resources Information Center (ERIC), PsychInfo, Scopus and ISI Web of Science using key terms focused on the specific search strategy (oral, mouth, oral cavity, intraoral, oral mucosa, cancer, malignancy, tumor, carcinoma, malignant, squamous cell carcinoma, prevalence, frequency, epidemiology, incidence, rate, trend, Saudi Arabia, Kingdom of Saudi Arabia). In addition, three key Saudi Journals (Saudi Medical Journal, Annals of Saudi Medicine, Saudi Dental Journal) were searched from their table of contents for relevant articles. No beginning

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date was used, and the last date of the search was Dec 30th, 2017. We searched for additional studies in the reference lists of all articles included.

Study selection

All the titles and abstracts were screened independently and in duplicate for inclusion in the study. The inter-rater agreement for study inclusion, as assessed using an intra-class correlation coefficient, was 0.79. Conflicts were resolved by consensus discussion between the two reviewers. Risk of publication bias was evaluated using Quality Assessment Tool for Quantitative Studies.^[15]

Data extraction

The Quality Assessment Tool for Quantitative Studies developed

for Effective Public Health Practice Project (EPHPP) as adopted by Thomas et al.^[15] was used to grade the methodological quality of included studies. The use of EPHPP tool is considered most appropriate for systematic reviews to assess intervention design variations for content and construct validity. The Tool also demonstrates excellent inter-rater reliability.^[15,16] This tool consists of six criteria: selection bias, study design, confounders, blinding, data collection method, and withdrawals/dropouts. According to the dictionary of the tool, each criterion was rated as strong, moderate, or weak; the overall assessment of the study is determined by assessing these ratings.

Data synthesis

The following data were extracted from each included study: first author, publication year, study type, study quality, sample

Table 1: Descriptive characteristics of studies included in the review.

Author /Year	Source of data/year	Sample size, OC prevalence/ Mean age	Male to female prevalence ratio	The common sites of OC	Most common Type of OC	Stage/Grade of OC	OC prognosis Recurrence/ Survival rate
Al-Idrissi/1990	KFH/1982-1989	Total cases 65, OC 21 (32.3%)/48.6 y	M – 64.6% F – 35.4%	T – 17% Others – 15%	SCC	Stage I – 16%, Stage II – 30%, Stage III – 38%, Stage IV – 13.8%, GI -21.5%, GII -36.9%, GIII – 41.5%	Survival at 1 y – 74%, 2 y – 26%
Cleatus/1992	KFH registry, Jizan/1983-1990	Total cancer 303, OC 208 (68.6%)/50-70 y range	F – 54.3% M – 45.7%	T – 42.8% FM – 20.7% BAM – 20.7% CM – 9.6%	SCC	T3N1M0 – 50.9% T2N1M0 – 31.7%	12.9% survival more than 5 y, 12% over 3 y survival, 3.8% less than 3 y survival
Allard /1999	TR data from KFSHRC/ 1976 - 1995	Total cancer-26510, OC-794 (35.4 % from Jizan)/ Mean age for OC 59 y	For OC overall SA 1.2:1, Jizan: 0.9:1	T- 52.14% LG – 20.02% CM – 13.85% FM – 8.18%	NA	NA	NA
Al-Rajhi/2002	KFSHRC/1992-1998	OC cases 57, Jizan (61.4%)/ Median age 65 y	M – 57.9% F – 42.1%	AR – 45.6% T – 38.6% BAM – 10.5%	SCC	Stage II – 8.8%, Stage III - 14%, Stage IV – 77.2%	5 y overall survival – 24%, Recurrence free survival – 14%
Al-Balawi/2002	RKH/1992-1999	OC cases 228/50.2 y	M – 65.3% F – 34.7%	T – 45% FM – 18.4% RMA – 15.35% LM – 10.5%	SCC	NA	56% of recurrence in 2 y post treatment
Brown/2006	NCR/1996-1998	OC cases 417, ASR 1.81/100,000 for M and 2.13/100,000 for F/Median age 62 y, Cases- 48, Controls-96/ Mean age for M – 56 y, F – 44 y	1:1, Jizan 0.7:1 (ASR 6.2/100,000 for males and 9.82/100,000 for females)	T – 69.6% F, 62.7% M,	SCC	NA	NA
Ali Quadri/2015	KFH registry, Jizan/ 2014	OC cases 417, ASR 1.81/100,000 for M and 2.13/100,000 for F/Median age 62 y, Cases- 48, Controls-96/ Mean age for M – 56 y, F – 44 y	M- 18.7% F – 14.6%	NA	NA	NA	NA
Idris/2016	KFH registry, Jizan/2009-2014	Total 714, OC -303 (42.4%)/ 65 ± 13.9	F: 63.4% M: 36.6%	BAM – 52.3% T or FM – 47.7%	SCC-85%, VC – 3.3%	GI – 32.2% GII – 53.9% GIII – 5.8%	NA
Qannam/2016	CD KSU registry/1984-2013	Total 231, OC 50 (21.6%)/69 y	1.4:1	AR – 39% T – 25%	SCC – 88%, VC – 8%	NA	NA

TR: Tumor Registry, OC: Oral Cancer, KFSH&RC: King Faisal Specialist Hospital And Research Centre, KFH: King Fahad Hospital, CD KSU: College Of Dentistry, King Saud University, RKH: Riyadh Al-Kharj Hospital Registry, NCR: National Cancer Registry, ASR: Age Standardized Rate, Y: Years, SA: Saudi Arabia, T: Tongue, AR: Alveolar Ridge, LG: Lower Gum, CM: Cheek Mucosa, FM: Floor of the Mouth, RMA: Retromolar Area, LM: Lip Mucosa, BAM: Buccal Alveolar Mucosa, GI: Grade I, GII: Grade II, GIII: Grade III, SCC: Squamous Cell Carcinoma, VC: Verrucous Carcinoma, M: Males, F: Females, * -P value < 0.05. NA: Not Available.

size, mean age, male to female ratio, and risk factor for OC, prevalence data, reported grading or staging of OC, site affected, recurrence or survival rate, and the authors' conclusion using data extraction sheet.

Results

Trail flow

Using our search strategy, we identified 76 articles with an additional six identified from our review of references and journal indices. From these, we identified nine articles for inclusion in the present systematic review [Figure 1].

Study characteristics and study quality

The data were available from the year 1982 to 2014. The number of oral cancer patients ranged from 21 to 794 (total n = 2126), with a mean of 236.2. The mean age of oral cancer involvement ranged from 48.6-years to 65-years. Male to female percentage varied from 36.6% to 65.3%. The tongue was the most frequently affected site by oral cancer. Squamous cell carcinoma was the most common type of oral cancer [Table 1].

Out of nine studies included in the review, eight were retrospective hospital record-based without any controls; one

Table 2: Causative factors for oral cancer, study quality and study conclusion.

Author/Year	Study type	Causative factor	Study conclusion	Study quality
Al-Idrissi/1990	R	Tobacco smoking – 41.5%, Shamma use (mean of 10 y) - 26.2%	Most of the cases reported in advanced stage, survival rate was less among shamma users	Weak
Cleatus/1992	R	Shamma use (94.7%)	Females more frequently affected than males and Shamma use main cause for OC	Weak
Allard /1999	R	Shamma use	High prevalence cases of OC from Jizan (35.4% of all referred cases), Shamma use most common cause	Moderate
Al-Rajhi/2002	R	Shamma use in 86%	High prevalence cases of OC from Jizan (61%), Mostly in advanced stage	Moderate
Al-Balawi/2002	R	Tobacco chewing use in 58%	Tobacco chewing is the main cause of OC, Prognosis poor in Shamma users	Moderate
Brown/2006	R	Shamma	OC is a significant public health problem for the residents of Jizan and the women of Najran	Moderate
Ali Quadri/2015	Case –control, Hospital based, 1 case; 2 controls	Shamma-OR- 20.14,3.95 Pipe smoking- OR - 4.20, Cigarette OR - 3.95, Khat OR – 0.48	Shamma is a major threat for OC occurrence in the Jizan region	Strong
Idris/2016	R	Shamma alone – 45.3% OC, Non Shamma users – 54.7%	SCC most prevalent OC, Females more affected than males, Shamma use is the main risk factor	Moderate
Qannam/2016	R	NA	High prevalence of OC among geriatric population	Weak

R: Retrospective Hospital Based Study, OC: Oral Cancer, OR: Odds Ratio, SCC: Squamous Cell Carcinoma, NA: Not Available.

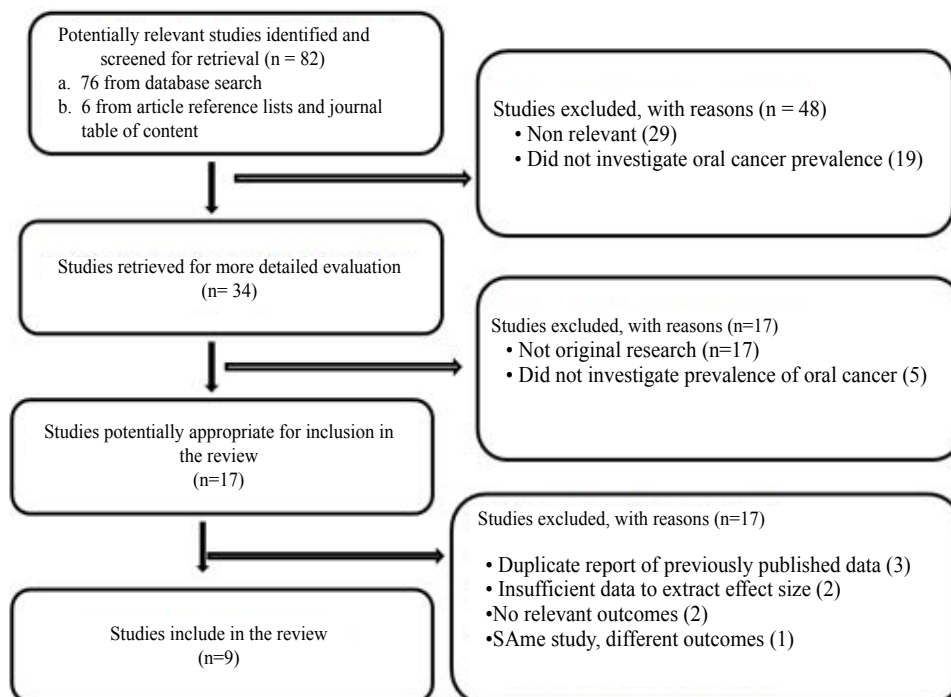


Figure 1: Study selection flow diagram of the systematic review.

was retrospective case-control study. Shamma use was the most frequent reason for oral cancer. The quality assessment rated one study as being of strong quality, five (55.6%) of the studies as being of moderate quality and three (33.3%) of these studies as being of weak quality [Table 2].

Discussion

Oral cancer is a public health problem in both developed and developing countries. It is one of the most common non-communicable diseases worldwide with an annual incidence of >300,000 cases. In Saudi Arabia it the third most frequent reason of malignancy after lymphoma and leukemia. The present systematic review is conducted to assess the prevalence and causative factors of oral cancer in KSA.

Prevalence of oral cancer

The present systematic review showed the prevalence of OC in KSA varied from 21.6% to 68.6%. It is a significant public health problem in the south of Saudi Arabia and specifically in Jazan province. Male to female ratio varied from 0.7:1 in Jazan province to 1.2:1 in other regions of KSA. The high prevalence of oral cancer among females may be attributed to increased consumption of smokeless tobacco Shamma which in-turn increased the risk of OC. This is in contrast to the recently published American Cancer Society 2017 report,^[17] which showed high prevalence of oral cancer in males compared to females.^[18-20]

Causative factor of oral cancer

In all of the included studies, the use of Shamma was the main reason for OC. Shamma is a preparation of smokeless tobacco,^[2-5] being a mixture of powdered tobacco, carbonate of lime, ash, black pepper oils and flavoring. The use of Shamma in the KSA is most commonly practiced in Jazan province, although it is not limited to this province.^[2,4,6,8,9] Shamma is also used in Yemen,^[3,8,21] which borders the KSA at Jazan province. Both *in vivo*^[18,22] and *in vitro* studies^[23] proved the role of Shamma in the induction of oral cavity tumors.

Common site of oral cancer

Results of this study showed that the tongue is the most commonly involved site in oral cancer. The results are in line with the studies from Asia and Europe.^[1,18-21]

Survival rate among oral cancer patients

The survival rate of oral cancer depends on stage or grade at which patient report to the hospital. In all of the included studies, the patients visited the hospital at the advanced stage of OC (Stage III and IV), so the five-year survival rate varied from 12.9% to 24%.

The limitation of the present review was, due to heterogeneity across the studies, we could not do the meta-analysis of included studies. Therefore, no forest plots or funnel plots were constructed. Due to the disparate nature of the studies, only simple descriptive and stratified comparisons are reported. Because of retrospective design of the included studies, it is difficult to get a firm conclusion.

Conclusions

- Oral cancer prevalence in KSA ranged from 21.6% to 68.6%. High prevalence of OC in Jazan province (32.1% to 62.4%).
- Shamma use was the main causative agent for oral cancer.
- Most of the OC patients reported to the hospital at advanced stage (Stage III and Stage IV) of the disease.
- The tongue was the most frequently affected site with OC, followed by the floor of the mouth and alveolar ridge.
- Five-year survival rate varied from 12.9% to 24%.
- There is a need for well-designed case-control studies to prove the role of Shamma in oral cancer.

Conflict of Interest

The authors disclose that they have no conflicts of interest.

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