# Epidemiology of oral cancer in Arab countries

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## ABSTRACT

**الأهداف:** إعادة النظر في دراسات سرطان الفم (OC) التي أجريت في الدول العربية فيما يتعلق علم الأوبئة، وعوامل الخطر، والتشخيص.

**الطريقة:** اعتماداً على الحاسوب لاستعراض الدِّراسات التي حصلت في الوطن العربي. وبعدَ استكشاف معايير الاستبعاد والقيَام بالبحث في الإحَالات المرجعيَّة والمجلاَّت المحلِّية، أُدْرِج مَجْموعة 19 مقالةً في هذه المَراجعة.

**النتائج:** ثمان دراسات خاصَّة بالانتشار بأنَّ معدَّلَ انتشار سرطان الفم كان ما بين 1.8 to 2.13 لكلّ 100,000. كما بحثت خمسُ دراسات في عوامل الخطر، في حين ركَّزت دراستان على عوامل المآل. وكان معظمُ مرضى سرطان الفم في العقد الخامس إلى السادس من العمر؛ وكان لدى اليمنيِّين أعلى نسبة انتشار بين الناس الذين تقل أعمارُهم عن 45 عاماً. كان هناك ارتباطٌ قوي بين المحدِّدات السُّلوكية، مثل التبغ غير المُدخَّن (الشَّمّ والقات على سبيل المثال) وتَدْخين السجائر، وسرطان الفم. كما ذُكر أنَّ شربَ الكحول والتعرُّض للإشعاع الشمسي هما من عواملَ الخطر المحتملة كذلك. وكانت المواضعُ الأكثر إصابةً هي اللسان وأرضيَّة الفم والشفة السفلية. كانت سرطَانه الخلايا الحرشفية هي السرطانَ الأكثر اكتشافاً في كثير من الأحيان، وكان المرضى في مراحل متأخِّرة عادة (على سبيل المِثال، المرحلة الثالثة والرابعة) في وقت التشخيص.

**الخاتمة:** لا توجد أدلَّةٌ ملموسة فيما يتعلَّق بمعدَّل انتشار أو وقوع سرطان الفم في معظم الدول العربية، نظراً لعدم وجود دراساتٍ قائمة على السكَّان أو سِجلاَّت وطنية عن السرطان.

**Objectives:** To review the oral cancer (OC) studies that were conducted in Arab countries with regard to epidemiology, risk factors, and prognosis.

**Methods:** A computer-based PubMed literature search was performed to retrieve studies conducted in the Arab world on epidemiology of OC. After screening for exclusion criteria, cross-referencing, and searching local journals, a total of 19 articles were included.

**Results:** Eight prevalence studies found an OC prevalence ranging from 1.8 to 2.13 per 100,000 persons. Oral cancer patients were mostly in their fifth to sixth decade of life, and the incidence in younger age was reported in some Arab countries. Yemenis have an alarming high prevalence of OC among people younger than 45 years. Eleven studies explored determinants or prognosis of OC. Behavioral determinants such as smokeless tobacco (Shamma and Qat), and cigarette smoking were strongly associated with OC. Alcohol drinking and solar radiation exposures were cited as possible risk factors. The most affected sites were tongue, floor of the mouth, and lower lip variations in the affected site were attributed to the socio-cultural behavior of the populations under study. Squamous cell carcinoma was the most frequently detected cancer, and usually patients were in late stages (III and IV) at the time of diagnosis.

**Conclusion:** No solid evidence exists regarding the true OC prevalence/incidence in most Arab countries due to the lack of national cancer registries and population-based studies.


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Oral cancer (OC) is defined as a neoplasm involving the oral cavity, which begins at the lips and ends at the anterior pillars of the fauces.[1] Globally, OC is reported to be the eighth most commonly diagnosed cancer with an annual incidence of >300,000 cases.[2] Incidence and mortality of OC are higher in developing countries when compared with developed countries.[2,3] Global prevalence of OC shows wide variation in the geographical distribution. For instance, OC prevalence

in the Indian subcontinent was 25% of all new cancer cases.[4] A noticeable increase in the prevalence of OC was noted in some industrial countries (namely, UK, Netherlands, and Denmark)[5,6] whereas other industrial countries (namely, Germany, France, Italy, Hong Kong, and USA) reported a decrease in the prevalence of OC.[7] In 2010, the World Health Organization (WHO) reported an OC mortality rate of approximately 2 per 100,000 in the Middle East, which is lower than that reported in India and the United States.[8] Squamous cell carcinoma (SCC) comprises 90-95% of all OC malignancies. In oral squamous cell carcinoma (OSCC), regional metastasis is prevalent in at least 30% of cases.[9] It develops mainly between the sixth and the seventh decades of life and occurrence in younger people (<40 years old) is rare.[10,11] Oral squamous cell carcinoma accounts for 4 of all malignancies in male and 2% in female.[12] Higher proportions of OSCC, in addition to an alarming rise in incidence among young people are being documented worldwide.[5,13] The most frequently affected sites of OC in Western countries are ventro-lateral aspects of the tongue and floor of the mouth, accounting for more than 50% of cases.[12] Conversely, in the southeastern part of the Asian continent, OC is significantly higher in buccal and commissural mucosa. This was attributed directly to the use of unrefined topical tobacco, being chewed or kept in the mouth for long periods.[14] The etiology of OC is multi-factorial comprising genetic, social, behavioral, and environmental risk factors. The major etiologic factors in the genesis of OC are tobacco chewing and/or smoking, and alcohol consumption.[15] Human papillomaviruses (HPVs) have been considered as etiologic agents, particularly in OC with no tobacco or alcohol association.[16] Potentially malignant disorders often precedes OSCC, and those showing features of moderate or severe epithelial dysplasia carry the highest risk for malignant transformation.[17]

The greatest challenge is that OC is not detected early enough for successful treatment, despite the fact that OC is mostly a visible lesion. Most dentists or general medical practitioners misdiagnose OC for more innocent lesions that show similar clinical appearance.[18] The aim of this article is to summarize the OC studies that were conducted in the Arab countries in regard to epidemiology, risk factors, and prognosis.

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**Methods.** An electronic search was conducted to identify articles in PubMed that met our inclusion criteria. The following key words were searched: diagnosis, distribution, epidemiology, factor, incidence, odds, pattern, prevalence, rate, risk, trend of OC, and each of the names of the 22 Arab countries (namely, Jordan, Egypt, Lebanon, Saudi Arabia, and so forth). Inclusion criteria were articles written in the English or Arabic language, epidemiological, and related to OC in the Arab world. Case reports and clinical trials regarding treatment options were excluded. Study was conducted in the College of Public Health and Health Informatics, King Saud bin Abdulaziz University for health Sciences, Riyadh, Saudi Arabia.

A total of 30 articles met the inclusion criteria dating back to 1985. Titles were reviewed to scan for exclusion criteria and 5 articles were excluded at this stage. Abstracts were reviewed and 3 articles were excluded. Full texts were then retrieved for 22 articles for careful reading, and evaluation; 6 more articles were excluded, leaving 16 articles to be included in the study.

A secondary search was performed by cross-referencing and supplementary electronic search in a number of databases using combinations of relevant key words. Searching local specialized journals in Arab world was performed as well. The secondary research identified 3 more articles that were not retrieved in our original PubMed search (**Figure 1**).

Data was retrieved, tabulated and processed using Microsoft Excel for Mac, version 14.5.9. No ethical approval was needed as no human participants were involved.

**Results.** In this review, we included 19 articles that discussed the incidence, prevalence or risk factors of OC in the Arab world. Most studies (n=11) used hospital or laboratory records as a source for the OC data (**Table 1**). Studies were grouped according to epidemiological focus research on OC.

***Prevalence and incidence studies.*** Studies were conducted in the following countries: Saudi Arabia, Jordan, Sudan, Libya, Yemen, UAE, Syria, Arab population living in Israel, Egypt, and Iraq.[19-29] They were cross-sectional studies and sample size ranged from 71 to 1787 patients.[19-28] All of these studies except one study from Saudi Arabia had used histological verification.[26] The incidence of OC varied greatly from 0.5/100,000 in Syria[19] to 10/100,000 in the Southern parts in Saudi Arabia,[26] with great regional variations among Saudi population in the same study. Two studies from Saudi Arabia[26] and Yemen[29] found a higher prevalence of OC among females. Conversely, all other

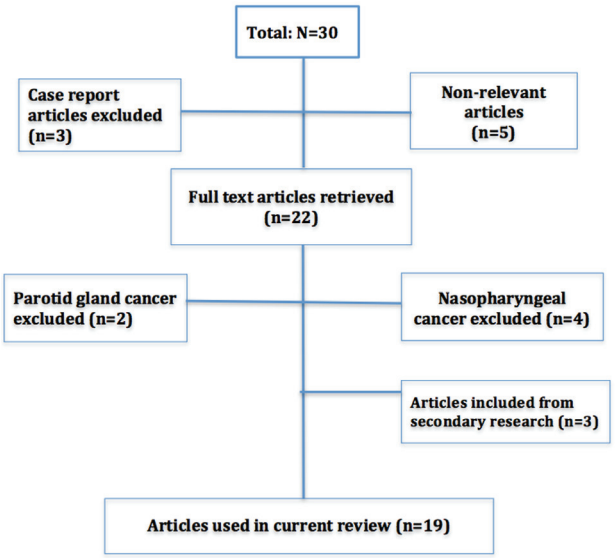


**Figure 1 -** Flowchart for research methodology in PubMed and supplementary search.

studies[18,19,21-23,25,27,28,30] reported higher ratio of males compared with females. **Table 1** provides a summary of the epidemiological indicators as measured in the included studies; namely, incidence, prevalence, mean age at diagnosis, histological types of OC, risk factor distribution, and prognosis.

The distribution of affected sites varied between Arab countries, but tongue and lips were the most affected sites in most studies (**Figure 2**). Uniquely, the gingiva and alveolus were the most commonly affected sites among patients from Southwestern region of Saudi Arabia (namely, Jizan and Najran).[31] Furthermore, in Sudan, a high presentation of overlapping lesions that exceeded one anatomical area to invade the adjacent one was observed.[24] Oropharynx was associated with the highest distribution of lesions among Arabs population residing in Israel.[27] The clinical features of OC were documented by some studies; swelling and/or ulceration were the most common clinical symptoms among OC patients,[21,24,25] White mucosal patches and lumps were less frequently encountered.[21,25]

*Risk factors studies.* A variety of tobacco habits were investigated in reviewed studies. Cigarette smoking was practiced by >50% of OC patients in Libya,[18] Iraq,[25] and Egypt.[28] Use of Shamma and Qat were related to the increased risk of OC in Saudi Arabia and Yemen.[29,32,33] In Sudan, it was reported that Toombac dipping was practiced by 34% of OC patients.[24] In Jordan,[34] Narghile (water-pipe) smoking was significantly associated with OC diagnosis at younger age (45.2 years). Other risk factors associated with OC are summarized in **Figure 3**.

*Prognosis studies.* Oral cancer lesions were diagnosed at late stages (stage III or IV) in most studies (**Figure 4**). Five-year survival rates ranged from 20-59.4%[27,31] (**Table 1**). Alveolus tumors showed a better outcome when compared with the rest of oral cavity sites, overall survival (32%), and relapse free survival of alveolus tumors (26%) compared with 8% overall survival and 4% in relapse free survival ($p$<0.001).[31] Lip cancer, young age at diagnosis (<30 years), and females showed the highest survival in other studies.[27,35] In Saudi Arabia, recurrence of the disease was observed in 56% of patients over a period of 5 years following initial treatment. Notably, invasion was not deep despite large tumor size among those with history of Shamma use.[36]

**Discussion.** This review article summarizes evidence in the etiology and prognosis of OC from 19 studies that were conducted among Arab populations. The prevalence of OC was the highest in countries/regions where tobacco-chewing habits are popular. This explains the high rates of OC among both gender in the Southwestern regions of Saudi Arabia, where Shamma and Qat use is a culturally accepted, and possibly encouraged, habit. Population of neighboring Yemen, who exhibited a similar high OC prevalence and a younger age at diagnosis, share these practices. The social popularity of such tobacco chewing habits encourages the uptake of habit among younger people. Early and continuous use of Qat was quoted as one reason for the high OC prevalence in Yemen.[3,29,37] Previous research showed that in Sudan OC is the fifth most common cancer, comprising 9% of the OC cases reported annually in Africa.[37] Findings from this review highlighted that presence of overlapping lesions were evident among Sudanese population.[24] This is strongly attributed to the use of local type of snuff known as Toombak, a very popular material in the Sudanese community that was established to contain high levels of carcinogens.[38,39] Public health efforts should strive to address these habits in their local communities as an attempt to reduce OC incidence. Anti-tobacco efforts should highlight the increased risk of OC and advise long-term tobacco users of seeking annual oral screening from oral health professionals. Overall, males were more affected than females in the Arab world. The range of proportion was 1:1-3:2, this gender difference in OC could be due to the increased exposure of male to exogenous carcinogens. The particular contribution of smoking and alcohol as etiological factors was cited as the possible cause of difference in OC between males

**Table 1 -** Summary of 19 articles that discussed incidence, prevalence, or risk factors of oral cancer (OC) in the Arab world.

| Country | Author(s) | Year | Source of data | Prevalence | Incidence | Mean age at diagnosis in years± SD | Male to female ratio | Most prevalent histological type | Risk factors distribution among OC patients | Prognosis |
|---|---|---|---|---|---|---|---|---|---|---|
| Arab population in Israel | Zini et al[27] | 2012 | Israel National Cancer Registry | | | 54.4±20.8 | | SCC: 66.3% | | Five years survival: 59.4%, mean survival time: 3.8±4.9 years |
| Egypt | Ibrahim et al[35] | 2009 | Hospital Records | | | 52.4±16 | 1.4:1 | SCC: 62.8% | | Twelve months survival rate: 76.5%, 5-year survival: 30.8%. Survival ranged between 36 and 46 months |
| | Labib et al[28] | 2012 | National Cancer Institute | | | 56.9±14 | 1.4:1 | SCC: 90% | Smoking (63.4%), spicy and hot foods (>3 times a day) (67.6%), and exposure to the sun (52.1%) | |
| Iraq | Alrawi & Talabani[18] | 2008 | Central Pathology Laboratory | | | 5th decade | 2:1 | SCC: 70%* | Heavy smoking (90%) | |
| | Museedi & Younis[22] | 2013 | Iraqi Cancer Registry | 2% from all cancers in 2000-2008 | | At the time of diagnosis: <60 | 1.3:1 | SCC: 91% | | |
| Jordan | Rawashdeh & Matalka[30] | 2002 | Regional histopathology laboratories | | | | 1.8:1 | SCC: 84% | | |
| | Al-Amad et al[34] | 2014 | Jordanian National Cancer Registry | | | 57.6 | Male: 68% | | Cigarette smoking (66%), narghile smoking (water pipe) (36%), alcohol drinking (17%) | |
| Libya | Jaber & Abu Fanas[25] | 2010 | Hospital records | | | 53 | 1.2:1 | SCC: 100% | Smoking 80% | Patients were diagnosed between 6-12 months of initial symptoms: 38.5% |
| KSA | Ibrahim[33] | 1985 | N/A | 59% among head & neck cancers | | | | | Shamma chewing (24.6%) or Shamma & Qat combination (33.8%) | |
| | Al-Ghamdi et al[32] | 1994 | Hospital records | 15% among head & neck cancers | 2.72/100000 year (for head & neck cancers) | 51 males, 52 females | Male: 54.3% | | | |
| | Al-Balawi & Nwoku[36] | 2002 | Hospital records | | | 23-82 (range) | Male: 65.4% | | Tobacco/Shamma chewing (58%) | Lesions among Shamma users were more resistant to radiotherapy/5-year recurrence: 56% |
| | Al-Rajhi et al[31] | 2002 | Hospital records | | | 65 (median) | Male: 58% | | | 5-years over-all survival: 20%, 5-year relapse free survival: 14% |
| | Brown et al[26] | 2006 | Saudi National Cancer Registry | | ASR of oral cancer was 1.81/100,000 for males and 2.13/100,000 for females | 62 (median) | | | Disparities in geographic locations: Jizan (male: 6.2/100,00 & female: 9.82/100,000) & Najran (female: 4.48/100,000) | Patients exhibited regional lymph nodes metastasis: 66% |
| | Halboub et al[20] | 2012 | Saudi National Cancer Registry | 5.28% of all cancer cases | ASR for Saudi males (2.4) was higher than non-Saudi males (1.6) | | | | | |
| Sudan | Osman et al[24] | 2010 | Hospital records | | | Male: 54.6 Female: 52.7 | 3:2 | SCC: 73.6% | Toombak users were (28.7%) and they exhibited overlapping lesions, smoking and alcohol use, 49% of patients traveled 5<hours to reach hospital | |
| Syria | Shahrour et al[19] | 2005 | Hospital records | | 0.5/100,000 | 54.3 | 1.8:1.2 | SCC: 60% | | |
| UAE | Anis & Gaballah[21] | 2013 | Hospital records | 15% of all biopsies | | 54.9 | | SCC: 62.3%* | | Neck metastasis: 44% |
| Yemen | Sawair et al[41] | 2007 | Hospital records | 18.3% of all primary cancers | | | | SCC: 84% | Tobacco chewers: 76.1%, Qat chewers: 59.8%, smokers: 23.9%, simultaneous chewing of tobacco and Qat: 52.2% | |
| | Halboub et al[42] | 2012 | Saudi and Yemeni Cancer registries | | | 58.2±14 | 1.24:1 | SCC: 55.5%* & 25.6%† | | Regional extension or metastasized lesions: 62% |

KSA - Kingdom of Saudi Arabia, UAE - United Arab Emirates, SCC - squamous cell carcinoma, ASR - age standardized rate, *well-differentiated, ‡moderately differentiated

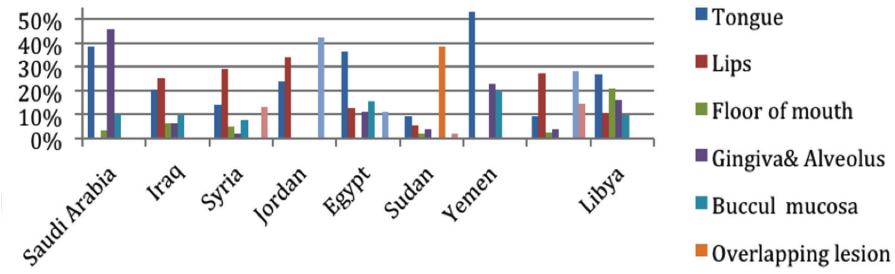


**Figure 2 -** Distribution of oral cancer lesions by Arab country.

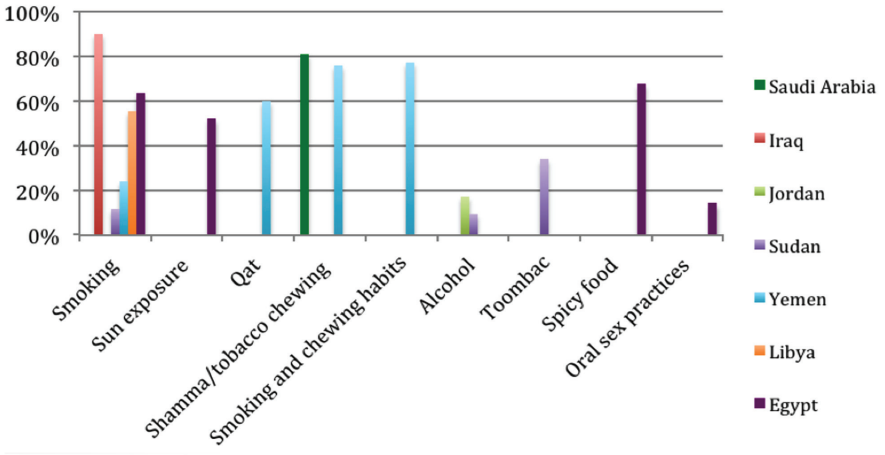


**Figure 3 -** Distribution of risk factors associated with oral cancer by Arab country.

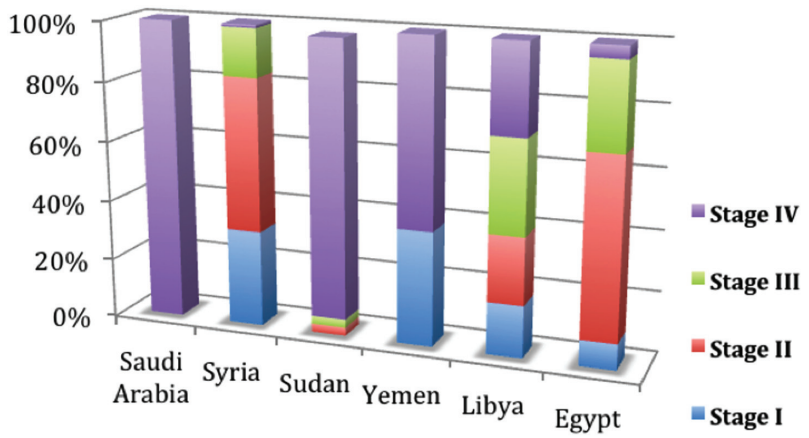


**Figure 4 -** Distribution of oral cancer histological stage at the time of diagnosis by Arab country.

and females,[40] as they are considered more stigmatizing for females in this part of the world. The increase in female OC affliction in Southwest areas of Saudi Arabia is a testament of cultural effect on epidemiology of OC, where Shamma and Qat use are socially acceptable for females.

Studies often utilized hospital records and/or histopathology reports for OC distribution. Data taken from such records might be representative of the regional distribution of disease, are not accurate for detecting prevalence and incidence measures. On the other hand, data from cancer registries tend to be more

standardized and informative of OC epidemiology compared with other cancers in a country. Although the incidence of OC in Arab countries, in most cases, is lower than the world-standardized rate; OC remains a highly lethal and disfiguring disease. Alarmingly, OC was diagnosed mostly at late stages; thus, affecting the prognosis negatively. Delays in diagnosis and treatment can decrease 5-years survival rate from 60% for T1 tumors to 20% for T4 tumors. Treatment of OC is resource-intensive and might not be available and/or accessible for all populations. Monitoring patterns/trends of late OC presentation through National Cancer Registries might be a useful tool for evaluating health services infrastructure in certain areas. Activating the role of dentists in early detection of OC should be emphasized, through oral tissues screening for high-risk patients and/or high OC prevalence areas.

Previous research had implicated human papilloma virus (HPV) as a risk factor for OC.[16] None of the reviewed studies had explored the prevalence of HPV among patients diagnosed with OC. Human papilloma virus prevalence varies between countries, and investigating it might illustrate the magnitude by which viral infection contribute to OC development in different populations.

This review provides a summary on OC epidemiology in some Arab countries, and is by no mean an exhaustive of OC epidemiology in Arab countries. Most studies utilized hospital records, they possibly overestimated the prevalence, and presented the severe cases that might not be representative of the source population. We think that we have captured the vast majority of studies conducted on OC epidemiology as the search for articles was conducted in Arabic and English languages. Although search was restricted to one database (PubMed), it was augmented by cross-referencing and local journals' search.

In conclusion, the pattern and frequency of OC in Arab countries is inaccurate with the lack of population-based studies. However, from current evidence it seems that prevalence of OC lies between Western and South-east Asian populations. It is relatively rare across the Arab countries with the exception of parts of Yemen and Saudi Arabia; this was attributed to the local habits of chewing tobacco and Qat. The increase in the incidence of OC in younger Yemeni population is an alarming problem that calls for more attention and awareness from the community and public health organizations.

The great challenge is the early detection of OC, which improves prognosis and quality of life. We suggest that OC screening of high-risk population is needed to decrease the severity of disease at diagnosis or diagnose potentially malignant lesions before malignant transition occurs.

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