# Oral and pharyngeal cancers in Yemen: a retrospective study

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# سرطانا الفم والبلعوم في اليمن: دراسة استعادية عصام صالح حلبوب، محمود عبد الحق، أحمد المنديلي

الخلاصة: أظهرت الدراسات المرتكزة في المستشفيات تواترات مرتفعة جداً نسبياً لسرطاني الفم والبلعوم في اليمن. وتقدر هذه الدراسة التواترات النسبية لسرطاني الفم والبلعوم بين مرضى السرطان في اليمن المسجلين في عامي 2007 و 2008، وتحدد السهات الديمغرافية للمرضى وسهات الورم. وقد بلغ عدد الحالات المسجلة 7515 حالة، منها 302 (4.0٪) لسرطان الفم، و239 حالة (3.2٪) لسرطان البلعوم. وقد كان سرطان الفم أكثر تواتُراً (تكراراً) بين النساء، كما كان سرطان البلعوم أكثر تواتُراً (تكراراً) بين الذكور. وكان مرضى سرطان الفم أكبر عمراً بقدر يُعْتَدُ به من مرضى سرطان البلعوم. وكان اللسان، كما كان سرطان البلعوم أكثر تواتُراً (تكراراً) بين الذكور. وكان مرضى سرطان الفم أكبر عمراً بقدر يُعْتَدُ به من مرضى سرطان البلعوم. وكان اللسان أكثر المناطق إصابةً في سرطان الفم (53.6٪)، بينما شكل سرطان البلعوم الأنفي 39.5٪ من سرطانات الأنهاط المورفولوجية شيوعاً سرطانة الخلايا الشائكة (3.9.2٪). وقد تم تشخيص نسبة مئوية من ويفعة من سرطانات البلعوم. وكان أكثر البلعوم (77.4٪) لدى المرضى في مراحل متقدمة. وبمقارنة النتائج مع ما لدى البلدان الأخرى في الإقليم، وجد الباحثون أن سرطاني العم والنات الأنفي يمثلان عبئاً ثقيلاً على الصحة الوطنية في اليمن.

ABSTRACT Hospital-based studies have revealed very high relative frequencies of oral and pharyngeal cancers in Yemen. This study estimated the relative frequencies of oral and pharyngeal cancers among Yemeni cancer patients registered in 2007 and 2008 and determined patients' demographic and tumour characteristics. Of the registered 7515 cases, 302 (4.0%) were oral cancer and 239 (3.2%) pharyngeal cancer. Oral cancer was significantly more frequent among females while pharyngeal cancer was significantly more frequent among males. Oral cancer patients were significantly older than pharyngeal cancer patients. The tongue was the most affected oral site (53.6%) while the nasopharynx comprised 89.5% of pharyngeal cancers. The most frequent morphological type was squamous cell carcinoma (93.2%). High proportions of oral cancer (71.5%) and pharyngeal cancer (77.4%) patients were diagnosed at advanced stages. Compared with other countries in the region, oral cancer and nasopharyngeal cancer represent substantial national health burdens in Yemen.

#### Cancers de la cavité buccale et du pharynx au Yémen : étude rétrospective

RÉSUMÉ Des études en milieu hospitalier ont révélé des fréquences relatives très élevées du cancer oropharyngé au Yémen. La présente étude a estimé les fréquences relatives du cancer de la cavité buccale et du pharynx chez des patients yéménites atteints de cancers enregistrés en 2007 et 2008. Leurs données démographiques et les caractéristiques de leur tumeur ont été relevées. Sur 7515 cas enregistrés, 302 concernaient des cancers de la cavité buccale (4,0 %) et 239 des cancers du pharynx (3,2 %). Les cancers de la cavité buccale étaient nettement plus fréquents chez les femmes alors que les cancers du pharynx étaient beaucoup plus nombreux chez les hommes. Les patients atteints d'un cancer de la cavité buccale étaient bien plus âgés que les patients souffrant d'un cancer du pharynx. La langue était le site le plus souvent touché de la cavité buccale (53,6 %) alors que le nasopharynx était impliqué dans 89,5 % des cancers du pharynx. Le type morphologique le plus fréquent était l'épithéliome malpighien (93,2 %). Des proportions élevées de patients atteints d'un cancer de la cavité buccale (71,5 %) ou du pharynx (77,4 %) ont reçu un diagnostic à un stade avancé de la maladie. Par rapport à d'autres pays de la Région, le cancer de la cavité buccale et du nasopharynx représente une charge sanitaire importante pour le Yémen au niveau national.

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#### Introduction

Oral and pharyngeal cancers were estimated to affect more than 482 000 people globally in 2008, more than half of whom (273 000) died of the disease [1]. Unfortunately, two-thirds of these cases occurred in developing countries [2]. The prevalence of oral cancer and pharyngeal cancer shows a wide disparity by sex [1,3] and geographical area [3,4]. While nasopharyngeal cancer is prevalent among the Chinese [5], oral cancer has been known to be prevalent in South Asian countries such as India [6] and Pakistan [7]. Worldwide variations in oral cancer distribution are believed to reflect different prevalences and patterns of risk habits such as *khat* chewing and waterpipe smoking [8-11].

Hospital-based studies have also revealed very high relative frequencies of oral cancer [12] and head and neck cancer [13,14] in Yemen, where such risk habits are also common. As yet there has been no national population-based cancer report issued by the National Oncology Center (NOC) though many years have elapsed since its establishment in 2002. The objectives of this study therefore were to determine the relative frequency of oral cancer and pharyngeal cancer among Yemeni cancer patients who were registered at NOC in 2007 and 2008 and to analyse these patients by demographic and tumour characteristics.

## Methods

This descriptive, epidemiological study was carried out on retrospective data provided by the NOC, Sana'a, Yemen. For all patients registered in 2007 and 2008, data regarding all patients with head and neck cancers was provided. The data included demographic details (sex, age and address) and tumour details (primary site, histology, grade and stage). The first author (H.E.) had access to the patients' hard files to validate the provided data. When there were discrepancies between data sources, the data in the hard files were used. The primary site (topography) and histology (morphology) of the neoplasms were reclassified and coded according to the International classification of diseases for oncology, 3rd edition (ICD-O-3) [15]. Hence only patients with malignant oral cancer or pharyngeal cancer (code C00-C14) were included in the present analysis. Tumours with other codes (i.e. not epithelial tumours) were excluded, even those affecting the oral cavity, pharynx or both sites. For the included cases, tumour staging was reclassified and coded according to the SEER summary staging manual 2000 [16]. The main morphology of the malignant tumours were reclassified further as: squamous cell carcinoma; adenoid cystic carcinoma; and papillary carcinoma. The less frequent morphological types were reclassified as other.

The statistical description and analyses were carried out using *SPSS* software, version 19. The descriptive statistics were presented as mean and standard deviation (SD) and relative frequencies as appropriate. The differences in age, were analysed by independent *t*-tests, while the associations of the cancer distribution (oral cancer versus pharyngeal cancer) with the different grouping factors were analysed using chi-squared tests. P < 0.05 was taken as the level of significance.

#### Results

Of the 7515 patients registered with neoplasms in 2007 and 2008, 1004 (13.4%) had head and neck cancers. Of these 541 were primary malignancies of the oral and pharyngeal tissues (code C00-C14); 302 (4.0%) were oral cancer and 239 (3.2%) pharyngeal cancer. Patients with tumours of the mesothelial and soft tissues (code C45-C49), lymphoid, haematopoietic and related tissues (C81-C96) and ill-defined secondary and unspecified sites (C76-C80) were erroneously registered as oral cancer or pharyngeal cancer and were excluded (n = 110).

#### **Distribution by site**

The tongue was the most affected oral subsite (162/302, 53.6%), followed by the floor of the mouth (55/302, 18.2%). Nasopharyngeal cancer constituted the major proportion of pharyngeal cancers (214/239, 89.5%) (Table 1).

#### **Distribution by region**

Of the 541 cases of oropharyngeal cancer 19.2%, 11.8%, 8.7% and 7.8% were referred from Al-Hodeida, Taiz, Hajja and Al-Amana provinces respectively (Table 2). The distribution of oral cancer and pharyngeal cancer was statistically different across different provinces (P < 0.001). Oral cancer was more frequent in Al-Hodeida, Hajja and Al-Mahweet provinces while pharyngeal cancer was more frequent in almost all other provinces.

## Distribution by age and sex

The overall mean (SD) age of oropharyngeal cancer cases was 52.8 (SD 17.0) years. Although the difference in age between males and females within each cancer type was not significant, oral cancer patients (males, females or both) were significantly older than their pharyngeal cancer peers (P < 0.001) (Table 3).

More males were affected by all oropharyngeal cancers (297, 54.9%) than were females (244, 45.1%) (Table 1). The male to female ratios for oral cancer and pharyngeal cancer were 1.0 (152:150) and 1.5 (145:94) respectively. There was also a difference in the distribution of oral and pharyngeal cancers by sex. Women were more susceptible to oral cancer and males to pharyngeal cancer (P = 0.016) (Table 4). Neither the subsite distribution of oral cancer

was significantly associated with patient's sex (Table 1).

One-quarter of oropharyngeal cancer patients (135, 25.0%) were aged  $\leq$  40 years. Significantly more of this younger group had pharyngeal cancer than oral cancer, whereas among the older age group pharyngeal cancer was more common (*P* < 0.001) (Table 4).

# Distribution by grade and stage

It is noteworthy that all cases were histologically verified. The most frequent morphological type of oropharyngeal cancer was squamous cell carcinoma (93.2%) and this was true for both oral and pharyngeal cases. The distribution by histological grade was significantly different; more of the well- and moderately-differentiated cancers were in oral cancer (258/302, 85.4%) compared with pharyngeal cancer (32/239 13.4%) (P < 0.001) (Table 4).

A high proportion of both oral (216, 71.5%) and pharyngeal (285, 77.4%) cancer patients were diagnosed at advanced (regional/metastasized) stages; however, the proportion of pharyngeal cancer patients at an advanced stage was significantly higher (Table 4) (*P* < 0.001).

#### Discussion

The cancer registry is an essential part of any rational programme of cancer control, benefiting both individuals and the society in which they live. Establishing the NOC was therefore a big step towards improving cancer control in Yemen. Nevertheless, providing chemotherapy and radiotherapy to patients has been the main priority of the health service and the work of the registry centre has been neglected. Hence, many patients with early stage cancer or who had chemotherapy elsewhere might not have been recorded. Additionally, many cancer patients in Yemen still prefer to go abroad for treatment and are consequently not recorded. Therefore it would have been unreliable to attempt to calculate the cancer incidence in this study as it would have been an underestimate. The relative frequency is still a valid measure, however. The comparison of relative frequencies of a given cancer between populations is at best an indirect measure of the absolute risk difference and will be more reliable when the cancer site of interest accounts for a small proportion of all cancer cases [17] as it is the case in the present study.

Another limitation of the present study was the quality of the provided data. No data on patients' habits were available. Moreover, there was no standard coding and classification of tumour topography, morphology and extent of disease at the time of diagnosis. The authors, however, made efforts to compare the provided data with what was recorded in the patient's files and recoded them according to the international standards. In addition, all the registered cases were histologically verified which makes the present data reasonably valid and reliable.

The present analysis contradicts hospital-based studies which reported higher relative frequencies of oral cancer in the central and northern regions of Yemen: 18% [12] and 8.7% [14]. However, the figure in this study slightly exceeds what was previously reported in the southern region of Yemen: 2.9% [18]. Such a regional disparity within an individual country was reported previously in Yemen [19] and Saudi

Table 1 Subsite distribution of 541 cases of oral cancer and pharyngeal cancer by sex							
Cancer type	Total ( <i>n</i> = 541)		Males ( <i>n</i> = 297)		Females ( <i>n</i> = 244)		
	No.	%	No.	%	No.	%	
Oral cancer							
Lip	36	6.7	19	6.4	17	7.0	
Tongue	162	29.9	88	29.6	74	30.3	
Gum	37	6.8	15	5.1	22	9.0	
Floor of mouth	55	10.2	27	9.1	28	11.5	
Other & unspecified parts of the mouth	3	0.6	0	0.0	3	1.2	
Parotid gland	3	0.6	0	0.0	3	1.2	
Other & unspecified major salivary glands	6	1.1	3	1.0	3	1.2	
Subtotal	302	55.9	152	51.2	150	61.4	
Pharyngeal cancer							
Tonsil	8	1.5	4	1.3	4	1.6	
Nasopharynx	214	39.6	134	45.1	80	32.8	
Hypopharynx	17	3.1	7	2.4	10	4.1	
Subtotal	239	44.2	145	48.8	94	38.5	

Table 2 Distribution of 541 cases of oral cancer and pharyngeal cancer by province						
Province	Total ( <i>n</i> = 541)			cancer 302)	Pharyngeal cancer ( <i>n</i> = 239)	
	No.	%	No.	%	No.	%
Al-Hodaida	104	19.2	76	25.2	28	11.7
Taiz	64	11.8	30	9.9	34	14.2
Hajja	47	8.7	36	11.9	11	4.6
lbb	32	5.9	16	5.3	16	6.7
Al-Amana	42	7.8	12	4.0	30	12.6
Sana'a	36	6.7	14	4.6	22	9.2
Dhamar	35	6.5	20	6.6	15	6.3
Amran	31	5.7	12	4.0	19	7.9
Al-Mahweet	28	5.2	20	6.6	8	3.3
Aden	19	3.5	12	4.0	7	2.9
Other provinces	103	19.0	54	17.9	49	20.5
Total	541	100.0	302	25.2	239	11.7

Chi-squared test, P < 0.001.

Arabia [20]. In support of GLOBO-CAN estimations [21] and other reports [3,22–24], the relative frequency of oral cancer in Yemen was higher compared with many other developed countries and indeed other Arab countries. However, it was still much lower compared with data from Myanmar [25], Pakistan [7] and India [26]. The widespread habit of betel quid chewing within Asian populations, in addition to smoking tobacco, alcohol consumption and poor oral hygiene, have been associated with high incidences of oral cancer [8,9]. Chewing khat, smokeless tobacco use (locally known as *shamma*) and waterpipe smoking (locally known as *mada'a*) are widely prevalent in Yemen and have been linked with oral cancer [10,11]. Further research on this is needed in Yemen.

Unexpectedly, the relative frequency of pharyngeal cancer was higher compared with other reports from Yemen [12–14,18] and other countries [7,23–29]. Nasopharyngeal cancer, which accounted for more than 89% of the pharyngeal cancers in the present study, is relatively common among Iraqi [21] and western North African men [30] and among the Chinese [5]. It is not considered to be a tobacco-related cancer [27]. However, genetic and infectious etiologies have been suggested [31].

In agreement with reports from Yemen [12,18,19], Saudi Arabia [23], Kuwait [27], Myanmar [25] and many other developed and developing countries [3], the tongue was the most affected oral subsite in men and women. Differences between regions have been reported however. In south central Asia, the buccal mucosa was the most affected site and this is consistent with being the site where betel quid is held when chewing [3,26,32]. In Iraq, the lip is reported to be the most affected oral site [33,34], while the gingiva is the predominant oral site in Zimbabwe [35]. Although it is not the main site in direct contact with *khat, shamma* or both, the tongue is considered to be a high-risk site for oral cancer [36].

To the best of our knowledge, this was the first study which reported the distribution of oral cancer and pharyngeal cancer among different provinces in Yemen. Relative to pharyngeal cancer, oral cancer was significantly more common in Al-Hodeida, Hajja and Al-Mahweet provinces. Interestingly these areas are those where *shamma* 

Table 3 Distribution of 541 cases of oral cancer and pharyngeal cancer by mean age and sex								
Sex	Oral cancer		Pharyng	<i>P</i> -value				
	No. of cases	Mean (SD) age (years)	No. of cases	Mean (SD) age (years)				
Male	152	59.5 (15.5)	145	45.9 (14.9)	< 0.001			
Female	150	57.3 (12.9)	94	45.3 (17.2)	< 0.001			
Total	302	58.4 (14.3)	239	47.7 (17.6)	< 0.001			

Independent t-test.

SD = standard deviation.

Table 4 Demographic and clinical characteristics of 541 cases of oral cancer and pharyngeal cancer							
Variable	Total ( <i>n</i> = 541)			Oral cancer ( <i>n</i> = 302)		Pharyngeal cancer ( <i>n</i> = 239)	
	No.	%	No.	%	No.	%	
Age group (years)							
≤40	135	25.0	46	15.2	89	37.2	< 0.001
> 40	406	75.0	256	84.8	150	62.8	
Sex							
Male	297	54.9	152	50.3	145	60.7	0.016
Female	244	45.1	150	49.7	94	39.3	0.016
Main morphology							
Squamous cell carcinoma	504	93.2	281	93.0	223	93.3	
Adenoid cystic carcinoma	9	1.7	6	2.0	3	1.3	> 0.05
Papillary carcinoma	12	2.2	8	2.6	4	1.7	> 0.05
Other	16	3.0	7	2.3	9	3.8	
Grade							
Well differentiated	224	41.4	211	69.9	13	5.4	
Moderately differentiated	66	12.2	47	15.6	19	7.9	
Poorly differentiated	29	5.4	17	5.6	12	5.0	< 0.001
Undifferentiated	114	21.1	7	2.3	107	44.8	
Unspecified	108	20.0	20	6.6	88	36.8	
Tumour extension (stage)							
Localized	34	6.3	30	9.9	4	1.7	< 0.001
Regional	334	61.7	193	63.9	141	59.0	
Metastasized	67	12.4	23	7.6	44	18.4	
Unspecified	106	19.6	56	18.5	50	20.9	

<sup>a</sup>Chi-squared test.

use and waterpipe smoking are known to be widely prevalent. As no data on substance use habits were available, future research could investigate whether these habits are associated more with oral cancer than pharyngeal cancer.

Both sexes in this study were found to be affected equally by oral cancer. Previous reports from Yemen [13,14,18] and other countries [3,7,23–26,34] found a higher relative frequency of oral cancer among men. However, Sawair et al. reported a higher relative frequency of oral cancer among women in Yemen [12]. Cultural norms allow more men to be exposed to risk factors for oral cancer such as smoking, khat and shamma compared with women and this is an area for future research. In agreement with studies in Yemen [12–14,18] and other countries [7,23–26,29], men more commonly were affected by pharyngeal cancer than were women. It is difficult at present to suggest reasons to explain the higher relative frequency of pharyngeal cancer (especially the nasopharyngeal cancer) among Yemeni men. However, face covers commonly worn by women in Yemen might protect them from infection by Epstein-Barr virus [31], which is considered as an etiological factor for nasopharyngeal cancer.

The mean age of oral cancer patients was comparable to those reported by previous studies in Yemen [12,19] and Iraq [33]. However it was lower than reports from Saudi Arabia [37] and most developed countries [38], but higher than reported in Pakistan [32], Myanmar [25] and Zimbabwe [35]. This disparity could be reflected partly by the onset and the intensity of practising risk habits in different regions worldwide. On average, the *khat* chewing habit starts in the early 20s and the frequency of practising it ranges from once a week to daily. *Shamma* use and waterpipe smoking, on the other hand, start at earlier ages and may be practised more than once a day.

Patients were affected by pharyngeal cancer at a significantly younger age compared with oral cancer. Moreover, more than 37% of patients with pharyngeal cancer were aged 40 years or less. The occurrence of pharyngeal cancer in younger age populations was reported too in Saudi Arabia [31] and Kuwait [27]. This might mean that the pharyngeal tissues are more susceptible or more exposed to risk factors or both.

In agreement with other studies in Pakistan [32], Myanmar [25] and Zimbabwe [35], squamous cell carcinoma was the most common morphologic type diagnosed in oral and pharyngeal cancers. Moreover, most oral cancer cases were graded well to moderate differentiation whereas most pharyngeal cancer cases were graded poor to undifferentiated. In addition to being more accessible to diagnosis, the previously mentioned findings might explain the lower proportion of oral cancer with advanced stage (regional and distant metastasis) compared with pharyngeal cancer. Unfortunately, only 9.9% and 1.7% of oral cancer and pharyngeal cancer cases respectively were diagnosed at the localized stage. These proportions might be underestimated; tumour stage was unknown in 18.5% and 20.9% of oral cancer and pharyngeal cancer cases respectively. Furthermore, many governmental and nongovernmental health facilities might not refer patients with early stage cancers to the NOC, leading to under-recording. However, patients' lack of awareness and health knowledge along with poor resources in primary and secondary health care are possible reasons that should not be overlooked.

A high relative frequency of pharyngeal cancer (especially nasopharyngeal) among Yemenis is noted here for the first time. Overall, nasopharyngeal cancer and oral cancer in Yemen represent national health burdens. Large-scale, matched case-control studies are needed to determine the risk factors for these cancers. The presence of a high quality national population-based cancer registry is the cornerstone to assess the burden of each site-specific cancer and to plan and direct the available health care resources and programmes accordingly.

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#### Cancer survival in Africa, Asia, the Caribbean and Central America

Population-based cancer survival rates offer an important benchmark for measuring a health care system s overall effectiveness in the fight against cancer. *Cancer survival in Africa, Asia, the Caribbean and Central America* presents in-depth cancer survival data from 27 population-based cancer registries in 14 low- and middle-resource countries.

The differences in cancer survival reported in populations observed between and within countries studied in this volume provide valuable insights for future planning and investment by governments in primary prevention activities, early detection initiatives and tertiary care to achieve meaningful cancer control.

Further information about this and other WHO publications is available at: http://www.who.int/publications/en/