

The unequal burden related to the risk of oral cancer in the different regions of the Kingdom of Saudi Arabia

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Objectives: To estimate the burden and risk of oral cancer in Saudi Arabia and highlight differences between regions. **Methods:** Using the National Cancer Registry Saudi Arabia, data was collated on numbers of cases of oral cancer (1996-1998) by site, age group, gender and region, plus relative frequencies of all cancer cases. Using Globocan, age-standardised rate (ASR) of oral cancer in Saudi Arabia was compared with five other neighbouring countries in the region. **Results:** A total of 208 lip, mouth and tongue cancers for men and 209 for women were reported to the registry during this period. ASR of oral cancer was 1.81/100,000 for males and 2.13/100,000 for females. It was ranked 15th most common cancer for males and 11th for females, with a ratio of 1:1 and median age at diagnosis of 62 years. Very wide regional disparities in the incidence of oral cancer were found, with an almost thirty-fold difference in ASR between the regions with the lowest and highest rates. Jizan Region had the highest ASR (6.2/100,000 for males and 9.82/100,000 for females). Here oral cancer was ranked 2nd for males and 1st for females, with a ratio of 0.73:1 and the median age at diagnosis for females was lower. The third highest ASR (4.48/100,000) was found in females in Najran. In these two high incidence regions oral cancer was commonly reported on the gingiva. **Conclusions:** Overall the burden and risk of oral cancer in Saudi Arabia are not large. However, cancer of the oral cavity is a significant public health problem for the residents of Jizan and the women of Najran. Saudi females in both these regions have a higher burden of oral cancer.

Key words: Incidence, oral cancer, Saudi Arabia, shamma, tobacco

Introduction

At the global level, non-communicable diseases have now replaced infectious diseases, maternal and perinatal conditions, nutritional deficiencies and injuries as major public health problems. Moreover, the burden attributable to cancer alone is expected to increase dramatically in the future due to growth and ageing of the world population and changing patterns of life-style. Thus, public health programmes specifically designed for the control of cancer are needed worldwide and populations at high risk identified.

Oral cancer most commonly arises in older males who are smokers, particularly when combined with excess drinking of alcoholic beverages (CRC, 2005). Smokeless tobacco is carcinogenic to humans, though wide variations in toxicity exist (Warnakulasuriya, 2004, Cogliano *et al.*, 2004) and in some populations it is noted that the risk is in excess for women than men (Gupta and Ray, 2003). There are known geographic, socioeconomic and ethnic disparities in the annual incidence of oral cancer (CRC, 2005; Moore *et al.*, 2000) that may be due to genetic differences but are more likely the result of social and cultural customs, particularly the use of different forms of tobacco rich in nitrosamines (Cogliano *et al.*, 2004). Morbidity and mortality from oral cancer are universally high and disproportionately so in developing

countries (IARC, 2004).

The Kingdom of Saudi Arabia occupies four fifths of the Arabian Peninsula, covering an area of approximately 2,250,000 sq km. The population is growing rapidly. The Central Department of Statistics estimates that approximately 22 million people presently live in the country of which almost three-quarters are Saudi nationals (Central Department of Statistics, 2003). The population age structure is typical of a developing nation with about 42.5% under fourteen years of age. This composition has an important bearing on the present pattern of cancer and possible future trends. As the country continues to modernise the total number of people will increase as will the proportion of older people. Consequently the cancer burden attributable to those cancers that for the most part affect the elderly will also grow.

Saudi Arabia is preparing to implement a National Cancer Control Programme (NCCP) under the auspices of the World Health Organisation (WHO). Analysis of the country's cancer burden and risk is an essential prerequisite. There have been a few regional projects investigating the epidemiology of oral cancer in the southwest of the country where the incidence is known to be high (Allard *et al.*, 1999; Papadakou-Sara, 1997) but, until now there has been no nationwide assessment of its burden and assessment of specific risk groups in Saudi Arabia. Use of smokeless tobacco (shamma) has

been suspected of causing cancer in parts of Saudi Arabia (Allard *et al.*, 1999; Hannan *et al.*, 1986; Papadakou-Sara, 1997).

Cancer is a mandatory notifiable disease in Saudi Arabia and thus the potential exists for comprehensive data collection. The National Cancer Registry (NCR), Saudi Arabia, was established by the Ministry of Health and has been gathering data since 1 January 1994. All Ministry of Health, Government and private hospitals as well as clinics and laboratories are required to report newly diagnosed cancer cases to their NCR regional branch or hospital office. The main NCR office is located at King Faisal Specialist Hospital & Research Centre (KFSH&RC) in Riyadh and is responsible for collating the data, assuring that there is no case duplication, cleaning and validating the data and preparing the bi-annual Cancer Incidence Reports. The data are entered into the CanReg 3.21 computer software programme provided by the International Agency for Research on Cancer (IARC), Lyon, France.

The objective of the study was to undertake a secondary analysis of the epidemiology of oral cancer in Saudi Arabia using the database at the National Cancer Registry in Saudi Arabia.

Method

The numbers of new cases of oral cancer (ICD-10: C00, C02-C06) by site, age group and gender for each region, 1996-1998 were extracted from the records of the National Cancer Registry (2001). The registry also provided the 1997 population demographics of Saudi Arabia for each region by age group and gender.

The total number and relative frequencies of all oral cancer cases were tabulated showing age distribution of cancer cases (1996-1998) by site and gender in the thirteen regions (Eastern, Madinah, Northern, Jof, Tabuk, Riyadh, Qassim, Hail, Asir, Baha, Najran, Jizan and Western) to identify those regions of highest incidence. The rates were standardised to the world standard population to estimate the age-standardised rates (ASR) for the country overall and each region individually.

The mean age at diagnosis and average annual age-specific rates (AIR) were also calculated, as were the relative frequency of cancer of the lip (C00), tongue (C02) and mouth (C03-06) by gender and region.

Data analysis

Assessing the statistical significance of the difference between rates from two regions was done by the Standardised Rate Ratio (SRR) method, i.e. the standardised rates and the associated standard errors were used to obtain an approximate confidence interval for the SRR using a method reported by Miettinen (1972).

Relative frequencies of all cancers in the country as a whole and the two regions with the highest incidence of oral cancer were taken from tables in the Cancer Incidence Report Saudi Arabia, 1997-98. The sites were then ranked to compare the rates for oral cancer with that for other cancers.

To allow comparison with neighbouring countries, the estimated age-standardised rates (ASR) of cancers

of the oral cavity (ICD9: 140-145) for the year 2000 in five of the Gulf Cooperation Council Countries (United Arab Emirates, Kingdom of Bahrain, Kingdom of Saudi Arabia, Sultanate of Oman, State of Qatar and State of Kuwait), were obtained from the age-specific incidence tables produced by the International Agency for Research on Cancer (IARC) available both on line www.iarc.fr and on the CD-ROM Globocan 2000.

The research study was approved by the Clinical Research Committee and the Research Ethics Committee, KFSH&RC Saudi Arabia (Project number 2031 036).

Results

From 1 January 1996 to 31 December 1998, 208 Saudi males and 209 females were diagnosed with oral cancer, a gender ratio of 1:1. Table 1 shows the regional variations in relative proportion of males to females. The ASR of oral cancer for the country as a whole was 1.81/100,000 for males and 2.13/100,000 for females. However, there were notable regional differences with the highest ASR found in Jizan, followed by Najran, Western then Eastern regions (Figure 1). The incidence rates of both genders in Jizan were significantly greater (95% CI male=(2.12 - 5.97), female=(3.54 - 10.24); $p < 0.05$) than those in Riyadh (the capital city), which were used as the Saudi standard; whilst among females in Najran the increase was only of borderline significance ($p=0.05$) and the 95% CI was 1.01 - 8.90. The ASR was significantly lower ($p < 0.05$) for both genders in Madina (95% CI male=(0.05 - 0.30), female=(0.09 - 0.57)) as well as Baha region (95% CI male=(0.14 - 0.89), female=(0.07 - 0.70)) and for males in the Qassim region (95% CI 0.16 - 0.82).

Overall the median age at diagnosis was 62 years for both genders but again there were regional disparities. The women of Jizan and Riyadh had the lowest median age of 57 years while men from Jizan and Najran reported a median age of 67 years.

For the years 1997 and 1998, cancer of the oral cavity was the fifteenth most frequently diagnosed cancer among Saudi males and tenth for females. The only region that showed a markedly different ranking was Jizan where oral cancer was the most common cancer among females and placed second for males (Table 2).

The average annual age-specific incidence rates of oral cancer increased fairly steadily and equally with advancing age among Saudi males and females (top panel of Fig 1) but in Jizan there was a consistently higher incidence among females than males until the age of 75 years (bottom panel of Fig 1). The curve representing annual average age specific incidence rate among females in Najran was close to that of Jizan males (Figure 1). Seventy to seventy-four year-old women from Jizan were the population group with the highest ASR throughout the whole country.

The tongue was the most common primary site of all oral cancers in the Western region; 62.7% of cases in males and 69.6% in females. In every other region, cancer of the mouth either predominated or was roughly equal to that of the tongue. Jizan showed a particularly high frequency of cancer of the mouth (62.3% for males and 65.8% for females) exceeded only by males in the

Table 1. Total number of cases of oral cancer, ASR and ratio of males to females in regions with 10 or more cases, 1996-1998

Region	Males	Females	M:F Ratio	ASR	
				Males	Females
Eastern	29	20	1.45:1	2.1	1.7
Madina	2	3			
Northern	0	0			
Jouf	2	2			
Tabuk	3	0			
Riyadh	34	27	1.26:1	1.7	1.6
Qassim	4	5			
Hail	3	1			
Asir	10	12	0.83:1	1.0	0.9
Baha	3	1			
Najran	6	9	0.67:1	2.7	4.5
Jizan	53	73	0.73:1	6.2	9.8
Western	59	56	1.05:1	2.1	2.4
Total	208	209	1:1	1.8	2.1

Table 2. Five most common cancers for males & females, Jizan Region, 1997-1998

Site	Males		Site	Females	
	Total	Relative frequency		Total	Relative frequency
Liver	33	16.1	Oral cavity	41	20.9
Oral cavity	23	11.2	Breast	30	14.6
Non-Hodgkin lymphoma	20	9.8	Ovary	17	8.3
Colon/rectum	12	5.9	Non-Hodgkin lymphoma	10	4.9
Bladder	10	4.9	Liver	8	3.9
Total	205		Total	206	

ICD 10 Codes: Liver = C22, Oral = C00-06 (Exc 01) , Non Hodgkin Lymphoma = C82-85, C96; Colon/Rectum = C18-21; Bladder = C67; Breast = C50; Ovary = C56

Eastern region (72.4%). When further broken down by subsite, it was found that oral malignancies in Jizan were most commonly reported on the gingiva.

The ASR of cancer of the oral cavity (ICD9: 140-145) in Saudi Arabia was found to be greater than in any of the other member countries of the Gulf Cooperation Council (Figure 2). It was the only Arab country to have a higher incidence among females than males.

Discussion

Secondary analysis uses data that the analyst was not responsible for collecting and forms an inexpensive method of data management for a research purpose or for health service research. However, the usefulness of the data collected by National Cancer Registries depends on its accuracy and completeness. The possibility that data is incomplete or inaccurate must always be borne in mind when using a registry for calculating cancer burden and risk. For example, a study of the cancer registry system in the southeast of England reported that although there was 95% completeness of registration for other cancers, oral cancer was under-reported, with 27% of diagnosed cases not included (Warnakulasuriya *et al.*, 1994). In 2003, Al-Zahrani *et al.*, (2003) published the results of their investigation into the completeness and validity of cancer registration in Saudi Arabia with the NCR during 1994, its first year of operation. Agreement was 95%

for laterality, 90% for primary site and 80% for basis of diagnosis. The authors suggested that these discrepancies were probably the result of inexperience and discussions with NCR staff confirmed that many of these difficulties had been resolved four years later.

Terminology and codes used for oral cancer reporting could be confusing (Moore *et al.*, 2000). When requesting data from the NCR, it was decided to use the definition of oral cancer given in the Joint Committee on Cancer, Cancer Staging Manual (1992), which excludes base of tongue and salivary glands. All data for Saudi Arabia and its regions in this report follow that definition. However, the sources referred to for ranking the relative frequency of cancers in Saudi Arabia and comparing the ASR of oral cancer in Saudi Arabia with its neighbouring countries employed slightly different definitions (IARC 2004). The inter country comparisons are valid as the same sites had been considered.

The ASR of oral cancer in Saudi Arabia was not high by global standards; it lay roughly between the rates reported in Northern America and the United Kingdom (IARC, 2001). The gender ratio of 1:1 and ASRs of 1.81/100,000 for males and 2.13/100,000 for females indicated a slightly greater risk of oral cancer for Saudi females. It was noted in the introduction that worldwide oral cancer is more common among males so this gender distribution is unusual. Otherwise, the median age at diagnosis of 62 years and the increased

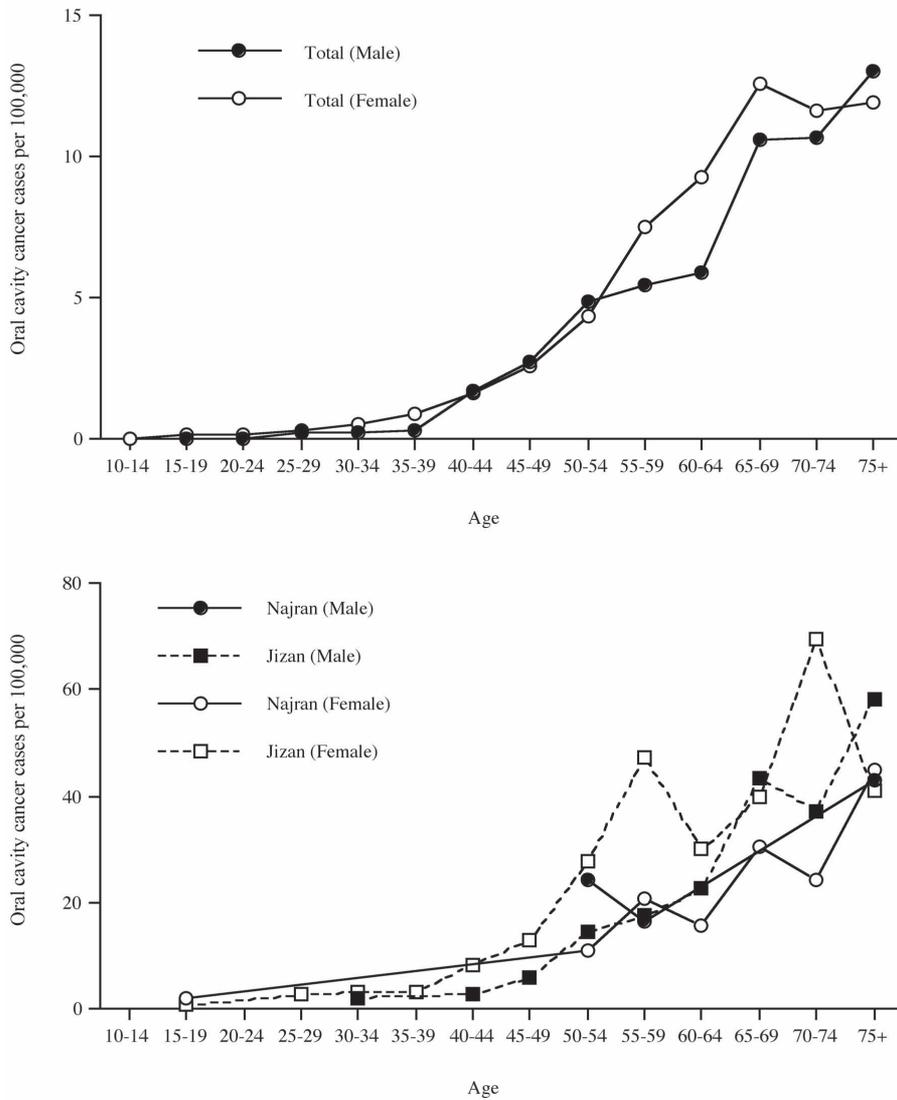


Figure 1. Incidence rates for oral cancer by age and sex: Saudi Arabia and its high incidence regions.

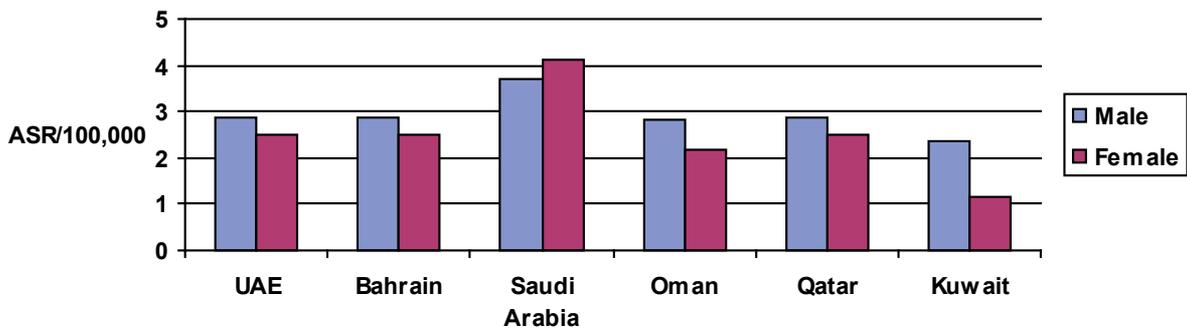


Figure 2. Oral cancer rates reported from member countries of the Gulf Cooperation Council (Source Globocan, 2000)

incidence with age for both genders were similar to most industrialised nations.

Taking Saudi Arabia as a whole, the relative frequency of oral cancer was ranked in fifteenth place for males and eleventh for females. Thus, the burden and risk of oral cancer in Saudi Arabia were low relative to other cancers but there was disproportionately high oral cancer rates in some regions.

As the country becomes more developed the population structure will alter and the number and proportion of older people increase (Khoja and Farid, 2000). Thus, it is likely the incidence of cancer, including that of the oral cavity, will also grow. So, although not at present a substantial problem in Saudi Arabia, it is recommended that oral cancer be included in the health education arm of the national cancer control programme with local poli-

cies in place for the high incidence regions.

One of the aims of this project was to highlight the inequality in oral cancer burden that exists between the regions of Saudi Arabia. Wide regional variations were found in the age-standardised incidence rate of oral cancer. There was an almost thirty-fold difference in the ASRs between the region with the lowest and that with the uppermost rate. While many countries have regional disparities, few are quite as extreme and striking differences in risk factors, such as use of a specific tobacco-product, have not reported. The considerably higher incidence in Jizan than elsewhere was striking although not unexpected; previous hospital-based studies (Allard *et al.*, 1999; Papadakou-Sara, 1997) had noted the high incidence in this region. However, the increased incidence among the females of Najran has not previously been reported.

Shamma, a smokeless tobacco product consisting of powdered tobacco, carbonate of lime, ash, black pepper, oils and flavourings (IARC, 2006), has been closely linked with the development of oral cancer (Hannan *et al.*, 1986). The use of shamma is socially acceptable, as well as widely believed to dull the pain of toothache and rapidly leads to nicotine dependence. Veiling also encourages women to retain the tobacco in their mouths for particularly long periods of time and this may explain the disproportionately higher incidence found in Saudi women. Shamma is easily obtained, even though illegal, in Saudi Arabia. It is manufactured locally or imported from Yemen and cheap to buy. Papadakou-Sara (1997) reported the highest consumption of shamma in Jizan occurred among females aged 35 to 64 years and males aged 50 to 74 years. The results for age specific incidence (Table 1) and the lower median age at diagnosis in females Jizan support this association.

Disparities in incidence and relative frequencies of cancer of the lip, tongue and mouth are usually due to differences in predominant risk factors. For most western populations tobacco and alcohol are the two major contributory agents acting either synergistically or independently (CRC 2005). Data on alcohol use in Saudi Arabia is not available and consumption of alcoholic beverages is illegal. The most likely variable in this population is different patterns of tobacco use. It is also possible that other risk factors might be involved, such as diet, genetic susceptibility, other unknown environmental carcinogens, viral infection (particularly the human papilloma virus), poor dentition or use of khat popular in neighbouring Yemen.

In India oral cancer is considered a substantial public health problem. The government and other agencies (IARC, AICR) have devoted considerable resources to its management. They have been successful with tobacco control initiatives (Shimkhada and Peabody, 2003) and introduced screening programmes aimed at reducing mortality in high-risk individuals (Sankaranarayanan *et al.*, 2005). Although not possible to make a direct comparison since the sites included in the assessments differed slightly, the estimated age standardised rate for cancer of the oral cavity in India was 12.8/100,000 for males and 7.5/100,000 for females while in Jizan it was 6.2/100,000 for males and 9.82/100,000 for females. Using the age standardised rate for males in Jizan the

rate was approximately half that for Indian males but for females about one and a third times greater. Thus, there is a similar need for an oral cancer control programme in the southwest region of Saudi Arabia.

In conclusion, oral cancer has a very severe impact on the health status of the people of Jizan while also seriously affecting that of the women of Najran. The concepts of community involvement focus on prevention and intersectorial cooperation enshrined in the principles of primary healthcare (Warnakulasuriya *et al.*, 1984; WHO, 1984) provide a good framework around which oral cancer management strategies could be developed in Saudi Arabia. Further research is also required on patterns of tobacco use in Saudi Arabia that are likely to underpin clear regional variations and also higher risk for oral cancer found in some Saudi women in this study.

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