

RESEARCH COMMUNICATION

Epidemiology of Oral and Pharyngeal Cancers in Khon Kaen, Thailand: a High Incidence in Females

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Abstract

Background: This study was aimed to describe incidence, trends, and survival of oral and pharyngeal cancers in Khon Kaen, the province situated in the northeast of Thailand. **Methods:** Data on oral and pharyngeal cancer cases diagnosed during 1985 - 2001 were retrieved from the population-based cancer registry of Khon Kaen. The final status of the patients was verified by database linkage and follow-up using postcards. **Results:** Of 1,038 cases, 62.6% were female and 37.4% were male, with a mean age of 63 years. The age-standardized incidence rate (ASR) in females (6.2 per 100 000; 95% CI 5.7-6.7) was significantly higher than in males (3.9 per 100 000; 95% CI 3.5-4.4). Annual percent changes in ASR were 1.7 in females ($p < 0.05$), but 1.2 in males. Lip and buccal cancers were the most common sites respectively; however, the incidence of tongue cancer was increasing in the last period. Eighty five percent of all cases were diagnosed in advanced stage (stage III and IV). The overall five-year relative survival was 43.1%. We found stage distribution and survival did not change during the study period. **Conclusion:** The considerably high incidence in female suggests a need for research on specific risk factors. Moreover, attempts should be made to detect oral cancers earlier in order to improve the outcomes of cancer control.

Keywords: Oral cancer - pharyngeal cancer - trends - incidence - survival - Thailand

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Introduction

More than 400 000 cases of oral and pharyngeal cancers diagnosed annually, with almost two-thirds of them found among male (Ferlay et al., 2010). Their incidence has increased in most countries over the last four decades (Posner, 2003).

Oral cancers including pharyngeal cancers are among the ten leading cancers in Thailand, with a typically higher incidence in males (Sriplung et al., 2005). However, in Khon Kaen, the incidence of oral cancer is uniquely higher among females, especially lip cancer, whose incidence was among the highest in women in the world (Ferlay et al., 2005). Knowing patterns of cancer occurrence in this area would not only reflect burden and outcome of oral cancer control, but also provide information to generate hypothesis for further studies on potential risk factors. Therefore, this study was aimed to describe incidence, trends in incidence, and survival of oral cancer in Khon Kaen using its population-based cancer registry.

Materials and Methods

Population and Registration procedure

Khon Kaen is the province situated in the center of

northeast Thailand, which covers an area of 13 404 km² with a population of 1.7 million (in 2002). Khon Kaen Cancer Registry was established in 1987 to collect data on all cancer cases in the province. Registration is mainly carried out by active methods by extracting data in medical records from all hospitals, including those from private and government sectors, and health promotion centers. The data from the years 1985-1986 were collected retrospectively from the same sources. Death certificates that mentioned cancer as a cause of death were obtained from the Office of the Chief Medical Officer and matched for cases outside the database. All data were verified, checked for duplication, coded, and entered into the database files using the CanReg4 program (IARC, 2007; Coleman and Bieber, 1991). Information was recorded on patient's sex, date of birth, date of diagnosis, method of diagnosis, site, extension, histology, date of last contact and vital status at last follow-up.

Data on all oral and pharyngeal cancer cases (International Classification of Diseases for Oncology (ICD-O): C00 - C14) excluding the major salivary glands (C07-C08) and nasopharynx (C11), diagnosed between January 1, 1985 and December 31, 2001 were retrieved from the population-based cancer registry of Khon Kaen.

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Follow-up methods

Follow-up was performed by both active and passive methods with December 31, 2002 as the last date of follow-up. The vital status of patients was initially verified with medical records and the death certificate database. A return-paid postcard was then sent to those whose status on the last date of follow-up was unknown from these sources, and re-sent to non-responders two months later.

Statistical methods

The age-standardized incidence rate (ASR) was computed by “direct method” (Silva, 1999) using the world standard population and reported as the number per 100,000 persons per year (person-year). The person-year at risk was calculated from annual estimates by age and sex, based on the censuses of 1990 and 2000. To determine the trends in incidence, the study period was divided into 4 four-year intervals from 1986 – 2001. The trends of incidence was obtained by calculating the annual percent change (APC) and tested for the difference from zero (p<0.05), using joinpoint regression program version 3.3.2 (Kim et al., 2000). The cumulative observed survival rates were calculated by the Kaplan and Meier method (Kaplan and Meier, 1958), and the cumulative relative survival rates were done by actuarial method. To determine the trends in survival, the study period was divided into 3 five-year intervals, excluding 1985 and 2001. STATA software 8.0 was used for all statistical calculation.

Results

Incidence and trends

Of a total of 1 038 oral cancer cases, 650 were female (62.6%) and 388 were male (37.4%). The mean age of patients was 63 years and ranged from 5 to 98. The overall ASR of oral cancer was 5.2 (per 100 000). The rate in females (6.2; 95%CI 5.7-6.7) was higher than males with statistical significance (3.9; 95%CI 3.5-4.4) (Table 1). The most common subsite in females was the lip, followed by the buccal mucosa, whereas in males it was the tongue, followed by the pharynx. About 77.5% of lip cancers occurred on the lower lip, 9.1% on the upper lip, and 0.4% at the oral commissure; the rest were unspecified or overlapping lesions.

The annual percent changes in the age-standardized incidence rates over the period of 1985-2001 were 1.21 per year (95%CI -1.5 – 4.0) in male and 1.67 per year

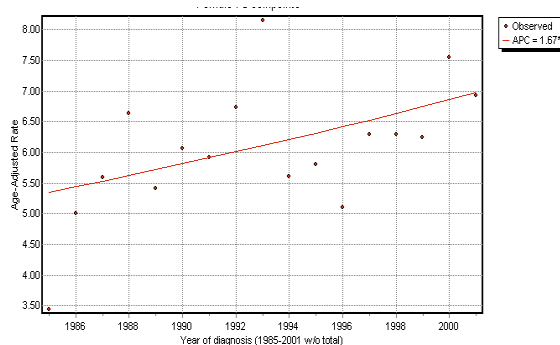


Figure 1. Annual Percent Change (APC) in the Age-standardized Incidence Rates in Females in Khon Kaen, 1985 – 2001

(95% CI 0-3.3) in females. The joinpoint analysis showed statistically significant increasing trend only in females (p<0.05) (Figure 1).

As we recruited cases from all levels of the health care units in the province, cancer diagnosis was verified by histopathology in 82.3 % of cases. Among these, the major cell type was squamous cell carcinoma (93.5%) followed by lymphoma (2.2%), adenocarcinoma (1.4%), undifferentiated carcinoma (1.2%), adenoid cystic carcinoma (0.9%), and others (0.8%).

We found ninety-five cases, or 9.2%, younger than 45 years, and 60% of them were male. The most common subsite was the tongue (30%), followed by the oropharynx (20%). In addition, the incidence was found to increase with age in both sexes.

Staging

Complete information on cancer staging was available in 44% of cases. About 85% presented in advanced stages (stage III or IV) in all subsites (Figure 3). Furthermore, we found that stage distribution did not change over time (data not shown).

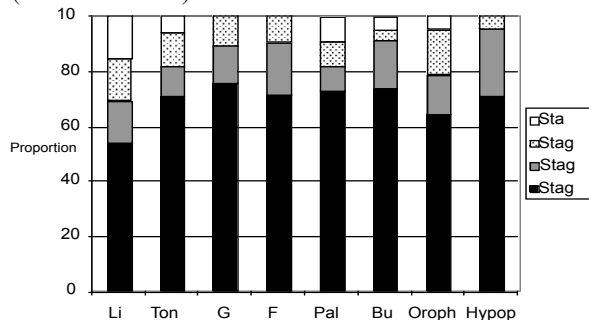


Figure 3. Stage distribution by Subsites in Oral Cancer, Khon Kaen, 1985 – 2001

Table 1. Incidence (ASR) and Proportion of Oral Cancers in Khon Kaen, 1985-2001, by Gender and Subsite

Subsite	Male			Female			Both		
	ASR	95%CI	percent	ASR	95%CI	percent	ASR	95%CI	percent
Lip	0.2	0.14-0.34	6.4	2.6	2.24-2.87	40.0	1.5	1.31-1.67	27.5
Tongue	1.1	0.87-1.29	27.8	0.8	0.62-0.96	13.4	0.9	0.79-1.06	18.8
Gum	0.4	0.24-0.49	8.5	0.5	0.39-0.68	8.6	0.5	0.36-0.55	8.6
FOM	0.3	0.19-0.41	7.7	0.2	0.08-0.23	2.6	0.2	0.16-0.29	4.5
Palate	0.3	0.17-0.39	6.7	0.2	0.08-0.23	2.9	0.2	0.15-0.28	4.3
Buccal & others	0.5	0.33-0.61	11.9	1.6	1.33-1.82	24.9	1.1	0.93-1.22	20.0
Oropharynx	0.6	0.41-0.71	15.2	0.3	0.19-0.40	4.9	0.4	0.33-0.51	8.8
Hypophaynx	0.6	0.47-0.81	15.7	0.1	0.07-0.21	2.6	0.4	0.28-0.45	7.5
Total	3.9	3.54-4.35	100.0	6.2	5.72-6.69	100.0	5.2	4.85-5.49	100.0

Table 2. Survival Rates by Subsite of Oral and Pharyngeal Cancer in Khon Kaen, 1985-2001

Subsite	Number of cases	Observed survival rate			Relative survival rate		
		1 yr.	2 yrs.	3 yrs.	1 yr.	2 yrs.	3 yrs.
Lip	285	82.1	65.8	56.0	87.3	77.3	73.3
Tongue	195	47.2	25.4	22.4	50.2	29.8	29.3
Gum	89	51.1	33.4	28.7	54.2	39.3	37.5
Floor of mouth	47	49.0	35.3	25.0	52.1	41.5	32.7
Palate	45	58.3	32.3	21.6	62.0	38.0	28.2
Buccal & others	208	54.8	40.9	33.7	58.2	48.0	44.1
Oropharynx	91	44.1	23.8	18.5	46.8	27.9	24.2
Hypopharynx	78	44.4	23.1	9.6	47.2	27.1	12.6
Total	1038	58.6	40.5	33.0	62.3	47.6	43.1

Survival

The overall five-year observed survival rate was 33% and relative survival was 43.1%. The best prognosis was found in lip cancer, whose relative five-year survival was greater than 70%. Although the survival of tongue cancer was found to be the least among oral cavities, those of oropharyngeal and hypopharyngeal cancers were far worse (Table 2). However, the survivals of oral and pharyngeal cancer were steady over the three-period of 1985 to 2000.

Response rate on follow-up procedure

After the death certificates were matched to the cancer registry and follow-up data from medical records were retrieved, 503 cases out of 1,038 cases were acquired for further active follow-up. Among these, 245 cases (48.7%) responded to the 1st post card. The following postcards were re-sent to 258 non-responders, and only 49 cases (20.0%) replied, leaving 208 unknown non-responders.

Discussion

This study showed that oral cancers were more common in females than males in Khon Kaen, with ASR of 6.2 and 3.9 (per 100 000) respectively. This finding contrasts to what have been reported from most countries worldwide. The global incidence of oral cancer in 2002 was 3.2 in females and 6.3 in males (Parkin et al., 2005), while, in Thailand, the ASR of oral cancers was 6.8 in males and 4.8 in females (Sriplung et al., 2005). According to the Cancer Incidence in Five Continents, lip cancer in female in Khon Kaen ranked the 3rd in the world, after Yukon of Canada and Tasmania of Australia (Ferlay et al., 2005). The different patterns of cancer incidence reflect different risk factors people exposed in different areas. Nevertheless, this requires a clear distinction between external (vermillion) and internal (mucosa) lips where their risk factors are dissimilar.

A case-control study in Khon Kaen found tobacco smoking, alcohol drinking, and be-tel quid chewing as major risk factors for oral cancer in both sexes (Vatanasapt et al., 1991). Additionally, more female habitually chewed betel quid than males in Khon Kaen, with a prevalence of 24 and 1.3 % respectively (Sriamporn et al., 2005). This is likely to account for higher incidence of oral cancer in female in this population, in particularly in elderly. We found more the lip and buccal mucosa (i.e. lateral lesions) involved in female, while the tongue, floor of mouth and

pharynx (i.e. central lesion) did in male. These findings are consistent to the study in Papua New Guinea, where oral cancer primarily located at the corner of the mouth and buccal mucosa, corresponding to the application of slaked lime and betel quid at this site (Thomas and MacLennan, 1992), as so did female in our study. On contrary, in US, where oral cancer strongly related to smoking and alcohol, found more tongue and pharyngeal cancers than those lateral lesions (Thomas and MacLennan, 1992), as so did male in our study. Likewise, a study in India shows proportion of tongue to non-tongue lesions of oral cancer in males was about 1:1, whereas that in females was 1:4 (Elango et al., 2006). This is also corresponding to the findings in southern India where 35% of oral cancer in males is attributable to combination of the smoking and alcohol, and 49% to pan-tobacco chewing, but 95% of those in females is explained by chewing and poor oral hygiene (Balaram et al., 2002).

The Global Alcohol Database showed Thai per capita consumption of pure alcohol increased from 0.26 litres per capita in 1961 to 8.47 in 2001, which become comparable with that of United States (FAO, 2003), may explain increasing cancer incidence of the tongue rather than lip and buccal mucosa. Although men are four times more likely to drink alcohol than women, the prevalence of female drinkers increased from 9.5 % in 1991 to 14.5 % in 2001 while that of men grew from 53.7 to 60.8 (Wibulpolprasert, 2005). In rural areas, alcohol used as tonics, i.e. bitters (liquor containing herbs), as well as traditional alcoholic beverages have prevailed; however, no study has ever been reported their prevalence and relationship to the cancers. Additionally, a study on herbal medicine spirit in Khon Kaen city detected chloroform, a possible carcinogenic to human (IARC, 1999), in 76% of the samples with the level of 0.04 – 0.12% by volume (Wangboonskul et al., 2003). More evidence has been found that Human papillomavirus become a risk factor for oral and oropharyngeal cancer, as the meta-analysis revealed a greater detection of this virus in oral squamous cell carcinoma than normal mucosa (OR 5.4, 95%CI 2.5 – 11.6) (Miller and Johnstone, 2001). These should be further investigated as a potential cause of higher incidence of oral cancer in females.

The overall five-year survival from our study was 43.1%, without significant improvement. It is between that of developing countries, e.g. India (39.7%) (Yeole et al., 2003), and that of developed countries, e.g. European Union (48.5%) (Coleman et al., 2003) and the United States (61.8% in whites and 39.5 in blacks) (Morse and Kerr, 2006) . This could mainly be explained by greater proportion of advanced stage cancer found in our population.

The ample room is still available to improve oral cancer control at all levels of strategies. For primary prevention, alcohol should be the greatest concerned as its prevalence is increasing, so is the incidence of tongue cancer, the site most related to all forms of alcohol (De Stefani et al., 1998; Johnson, 2001). Nevertheless, tobacco use should also be monitored and continued to counteract, as the new generation, particularly females, tend to smoke more (Wibulpolprasert, 2005). Likewise, the current

prevalence of betel quid chewing and its effect on oral cancers should be accurately determined. The secondary prevention is also remarkably important, since most cases still present at a late stage. Although the evidence is insufficient to prove the benefits of oral cancer screening at population level (Kujan et al., 2006), we recommend dentists and physicians to completely examine the oral cavity during their routine clinical service to detect any pre-cancerous or early cancer lesions. The causes of delay in diagnosis and treatment should also be explored and solved systematically. In spite of early stages, the oral cancer, particularly tongue, whose prognosis is relatively poor, should be treated in cancer care center where head and neck surgeon and radiotherapist are available, as the prognosis turns grave once tumor recurs. The quality of life should also be greatly concerned in cancer care where most cases are in advanced stage, since morbidity either the disease per se or treatments are substantial.

In conclusion, this population-based study showed an incidence of oral cancers and its trend in Khon Kaen significantly higher in females than males. The most common site in female was the lip, followed by buccal mucosa, whereas in males it was the tongue followed by the pharynx. The major problem is that most cases presented at a late stage. We suggest that early detection should be incorporated to routine clinical service, and that the parameters to identify gaps in the health care system, such as waiting time for diagnosis and treatment, should be monitored; and treatment especially of tongue cancer in a tertiary care units. Moreover, until we know what causes women to get more oral cancers in this population, further studies on their risk factors are required to address a unique burden of this cancer.

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