

**SURVIVAL AND PROGNOSTIC FACTORS OF  
ORAL CANCER PATIENTS IN HOSPITAL  
UNIVERSITI SAINS MALAYSIA, KELANTAN**

*by*

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## LIST OF ABBREVIATIONS

ACE-27	Adults Comorbidity Evaluation-27
BDA	British Dental Association
CDC	Center for Disease Control and Prevention
CI	Confidence Interval
cm	centimeter
df	Degree of freedom
HR	Hazard ratio
HRPZ II	Hospital Raja Perempuan Zainab II
HUSM	Hospital Universiti Sains Malaysia
ICD	International Classification of Diseases
LR	Likelihood Ratio
MC	Multicollinearity
MOH	Ministry of Health
SCC	Squamous Cell Carcinoma
SD	Standard deviation
SEER	Surveillance, Epidemiology, and End Result
SES	Socio-economic status
US	United States
USM	Universiti Sains Malaysia
VIF	Variation Inflation Factor
WHO	World Health Organisation

## **ABSTRAK**

### **TAJUK:**

Kadar jangka hayat dan faktor-faktor prognostik di kalangan pesakit kanser mulut di Hospital Universiti Sains Malaysia, Kelantan

### **PENGENALAN:**

Kanser mulut adalah penyakit yang boleh dicegah yang memberikan impak yang besar terhadap kematian dan keadaan tidak sihat serta kualiti hidup pesakit. Secara global, kadar survival lima-tahun untuk kanser mulut tidak berubah secara ketara, walaupun dengan kemajuan di dalam teknologi mendiagnosa dan merawat kanser mulut serta adanya pakar yang handal. Tujuan kajian ini adalah untuk meneroka survival dan mengenalpasti faktor-faktor prognostik yang boleh mempengaruhi risiko untuk mati di kalangan pesakit kanser mulut di Hospital Universiti Sains Malaysia (HUSM).

### **METHODOLOGI:**

Satu kajian semula rekod secara retrospektif telah dijalankan dari Ogos hingga Disember 2006, dengan melibatkan 133 pesakit yang telah didiagnosis sebagai pesakit kanser mulut dari tahun 1986 hingga 2005. Susulan tambahan selama satu tahun selepas pemilihan subjek telah dijalankan sejak 1hb Januari hingga 31hb Disember 2006, untuk menentukan status pesakit. Semua pesakit yang memenuhi kriteria dipilih memasuki kajian ini. Maklumat yang diperlukan semasa diagnosa dan status survival pesakit sehingga 31hb Disember 2006 telah disemak dari rekod perubatan oleh penyelidik utama. Maklumat berkenaan direkodkan ke dalam borang yang disediakan

husus, bagi memastikan pengumpulan data yang sama antara pesakit. Panggilan telefon dan lawatan ke rumah juga dijalankan untuk mendapatkan maklumat tentang status survival untuk pesakit yang masih hidup semasa keluar hospital tetapi gagal menghadiri temujanji dan tiada rekod susulan. Kemasukan data dan analisis telah dilakukan dengan menggunakan perisian SPSS versi 12 dan STATA versi 8. Kaplan-Meier telah digunakan untuk mengira anggaran survival sementara Cox Proportional Hazards Model menentukan faktor-faktor prognostik.

### **KEPUTUSAN:**

Kadar survival 5-tahun dikalangan pesakit kanser mulut di HUSM adalah 19.6% (95%CI:12.9, 27.2) dengan masa median survival selama 10 bulan. Dengan menyesuaikan pembolehubah yang lain, multivariable Cox Proportional Hazards Model, mengenalpasti faktor-faktor prognostik yang bermakna yang boleh mempengaruhi kematian akibat kanser mulut di in HUSM adalah umur semasa diagnosis (HR=1.02; 95%CI:1.00-1.03;  $p=0.004$ ), jantina (HR=0.61; 95%CI:0.40-0.95;  $p=0.028$ ), kehilangan berat badan (HR=1.74; 95%CI:1.13-2.64;  $p=0.012$ ), kesakitan (HR=1.64; 95%CI:1.01-2.66;  $p=0.045$ ), sakit telinga (HR=2.55; 95%CI:1.15-5.62;  $p=0.021$ ), TNM tahap III dan IV (HR=3.79; 95%CI:1.62-8.87;  $p=0.002$ ) dan rawatan (HR=0.32; 95%CI:0.21-0.49;  $p<0.001$ ).

### **KESIMPULAN:**

Survival dikalangan pesakit kanser mulut di HUSM boleh di katakan sangat rendah. Peningkatan umur semasa diagnosa, kehilangan berat badan, mengalami kesakitan, mengalami sakit telinga dan tahap TNM yang telah lanjut adalah faktor yang meramalkan keterukan risiko kematian akibat kanser mulut, manakala jantina



perempuan dan menerima rawatan adalah faktor pelindung terhadap hazard kanser mulut.

**Kata Kunci:** Kanser mulut, survival, prognosis, faktor prognostik, HUSM.

## ABSTRACT

### **Title:**

Survival and prognostic factors of oral cancer in Hospital Universiti Sains Malaysia,  
Kelantan

### **Introduction:**

Oral cancer is a preventable disease that gives high impact on mortality and morbidity as well as patients' quality of life. Worldwide, the five-year survival rate remained unchanged despite the advancement in the technology in diagnosis and treatment of oral cancer, as well as the highly experience specialist. The aims of this study were to determine the survival and to identify the prognostic factors that influence the risk of death of oral cancer patients in Hospital Universiti Sains Malaysia (HUSM).

### **Methodology:**

A retrospective record review was conducted from August to December 2006 in HUSM involving 133 patients diagnosed as oral cancer from 1986 to 2005. Additional follow-up of one year after the recruitment of the subjects was done from 1<sup>st</sup> January till 31<sup>st</sup> December 2006 to verify patients' status. All patients who fulfilled the inclusion criteria were included in the study. The required information at time of diagnosis as well as patients' survival status until 31<sup>st</sup> December 2006 was retrieved from medical records by the principle researcher and transferred to a specially design data extraction form. For some patients who were alive upon discharged from hospital but defaulted appointment or were loss to follow up, telephone calls and home visit were conducted

to obtain information on patients' survival status. Data entry and analysis was done using SPSS version 12 and STATA version 8. Kaplan-Meier was used to calculate survival estimates while Cox Proportional Hazards Model was used to determine prognostic factors.

### **Results:**

The overall 5-year survival rate for oral cancer patients in HUSM was 19.6% (95%CI:12.9, 27.2) with median survival time of 10 months. Adjusted for other variables, Cox Proportional Hazards Model identified the significant prognostic factors that influence death in oral cancer patients in HUSM as age at diagnosis (HR=1.02; 95%CI=1.00-1.03;  $p=0.004$ ), sex (HR=0.61; 95%CI=0.40-0.95;  $p=0.028$ ), weight loss (HR=1.74; 95%CI=1.13-2.64;  $p=0.012$ ), pain (HR=1.64; 95%CI=1.01-2.66;  $p=0.045$ ), earache (HR=2.55; 95%CI=1.15-5.62;  $p=0.021$ ), TNM stage III&IV (HR=3.79; 95%CI=1.62-8.87;  $p=0.002$ ) and treatment (HR=0.32; 95%CI=0.21-0.49;  $p<0.004$ ).

### **Conclusion:**

Oral cancer patients' survival in HUSM is very low. Older age at diagnosis, loss of weight, present of pain, present of earache, and advanced TNM stage were more likely to die due to oral cancer, while being female and received treatment, were protective factors. All these factors were considerably similar to other countries.

**Key word:** Oral cancer, survival, prognosis, prognostic factors, HUSM.

# **CHAPTER ONE:**

## **INTRODUCTION AND LITERATURE REVIEW**

### **1.1 ORAL CANCER**

Oral cancer is a malignant growth involving any of the oral cavity structure either the lips, tongue, salivary glands, buccal mucosa, gingiva, floor of the mouth, hard palate and retromolar trigone. It may arise as a primary lesion originating in any part of the oral cavity, by metastasis from distant site of origin, or by extension from neighbouring anatomic structure (CDC, 1996).

Oral cancer may originate from any of the tissues in the mouth, thus the histologic appearance may vary. The most common oral cancer is squamous cell carcinoma, originating from the tissues that line the mouth and lips. Other types of oral cancer are mucoepidermoid carcinoma, acinic cell carcinoma and adenocarcinoma derived from major or minor salivary gland, lymphoma from tonsillar or other lymphoid tissue, or melanoma from the pigment producing cells of the oral mucosa (Zakrzewska, 1999).

### **1.1.1 Incidence and prevalence of oral cancer**

Oral cancer was the sixth most common cancer worldwide, accounting for approximately 4% of all cancers and 2% of all cancer deaths (Worrall, 2001). Of 8.1 million new cases of cancer in 1990, 2.6% was oral cancer (Scully and Bedi, 2000). In 2002, 274,000 cases of oral cancer were diagnosed (Parkin *et al.*, 2005).

Globally, there was a marked variation in the incidence of oral cancer. National Cancer Institute, Surveillance, Epidemiology, and End Result (SEER) United State (US) data reported, the overall incidence rates for oral and pharyngeal cancer combined were 10.4 per 100,000 populations for the year 1991 (CDC, 1996). In 2006, Academy of Dental Therapeutics and Stomatology in US reported a lifetime risk of developing oral and pharyngeal cancer was 1 in 98 persons (Kerr, 2006). In the United Kingdom (UK), 4300 new cases of oral cancer were diagnosed yearly with 1,700 deaths toll (BDA, 2000).

Oral cancer was the most common cancer in India with prevalence up to 40% of all cancers (Zakrzewska, 1999) and accounting for a quarter of the world burden of oral cancer, 79,000 from a total 267,000 cases (Yeole *et al.*, 2003). In Sri Lanka, oral cancer accounted for 16.8% of all cancer cases for the year 2000 (Siriwardena *et al.*, 2006). In Thailand, oral cancer ranked fourth of the most common cancer in males and second in females. The highest incidence was reported in Songkhla with male incidence of 9.8 per 100,000 population for the year 1998 (Kerdpon and Sriplung, 2001).

In Malaysia, a national epidemiology survey of oral mucosal lesion reported oral cancer prevalence was 0.04% (Zain *et al.*, 1997). Another study among elderly population in Klang District showed higher oral cancer prevalence of 0.4% (Ali *et al.*, 1996). From 1994 to 1998, overall crude incidence rate was 0.74 per 100,000 population in Kelantan (Ghazali *et al.*, 2006). Penang Cancer Registry reported oral cancer accounted for 3% of all Penang Hospital cancer admissions in 1995 (Hooi and Devaraj, 1998). In 2003, 3.3% of all cancer in National Cancer Registry was oral cancer accounted for (Lim and Yahaya, 2004).

Looking at sex distribution of oral cancer, male was reported to have higher tendency in contracting oral cancer than female. The world area with the highest incidence was Melanesia with 31.5 per 100,000 in men and 20.2 per 100,000 in women. Rates in men were high in Western Europe (11.3 per 100,000), Southern Europe (9.2 per 100,000), South Asia (12.7 per 100,000), Southern Africa (11.1 per 100,000), and Australia/New Zealand (10.2 per 100,000). In females, incidence is relatively high in Southern Asia (8.3 per 100,000) (Parkin *et al.*, 2005).

In Malaysia, National cancer registry showed higher prevalence of oral cancer among female (51.3%) compared to male (48.7%) (Lim and Yahaya, 2004), consistent with data from oral cancer database and tissue resource bank, 2004, reported prevalence among female was 58.6% compared to 41.4% in males (Zain *et al.*, 2005). Mustafa *et al.*, (2007) also reported similar finding.

In US, distribution of incidence and prevalence of oral cancer showed that Black ethnic group was more affected compared to White ethnic group (CDC, 1996). As for Malaysian, the highest prevalence was 1.9 per 1000 population among Bumiputras, followed by Chinese with 0.4 per 1000 population and Malays with 0.3 per 1000 population (Zain *et al.*, 1997). However, more recent evidence showed Indians' male were ranked first of all cancer and second for female (Lim and Yahaya, 2004). Mustafa *et al.* (2007) and Zain *et al.* (2005) also reported highest prevalence of oral cancer among Indians.

Differences in age, sex and ethnic groups had a particular pattern in development of oral cancer. Older person were more likely to develop oral cancer compared to younger person (BDA, 2000). Men were 2 to 3 times more affected than women, largely due to high use of alcohol and tobacco (Johnson, 2001). Black group was more susceptible to develop oral cancer. However, in the absence of smoking, the rate of cancer was nearly equal for Black and White in US (Day *et al.*, 1993).

### **1.1.2 Mortality of oral cancer**

Mortality of oral cancer on average was less than half of the incidence (Parkin *et al.*, 2005). The US SEER data reported, the overall mortality rates for oral and pharyngeal cancer combined were 2.9 per 100,000 populations for the year 1991 (CDC, 1996). In 1996, the American Cancer Society estimated that of 1,200,000 new cases diagnosed and more than a half million would die (Worrall, 2001). In Japan, oral cancer mortality

was 3.3 per 100,000 population for the year 1990-1994 (Su *et al.*, 1999).

Females had lower mortality rate of 1.7 per 100,000 compared to 4.5 per 100,000 for males (CDC, 1996). A study in US reported the oral cancer mortality among males were 4.2 per 100,000 population compared to 1.6 per 100,000 populations among females for the period of 1995 to 2001 (Kerr, 2006). In the year 1980, oral and pharyngeal cancer caused 4.6% death of all cancers among Brazilian males compared to only 1.1% among females (Wunsch-Filho, 2002)

### **1.1.3 Risk Factors**

While the exact cause of oral cancer was unknown, several factors have been identified as contributing factors in the development of oral cancer. Tobacco and alcohol had the greatest impact on malignancy development. Tobacco used was associated with up to 12 times higher risk than the nonsmoking group (Ghali and Connor, 1999). Tobacco and alcohol interact synergistically to further amplify the risk of oral cancer (Robinson and Macfarlane, 2003). However, alcohol itself was not a strong risk factor. Its only raised the risk of oral cancer by three folds (Fioretti *et al.*, 1999).

In Malaysia and other Asian countries, chewing betel and areca nut had been known to be a strong risk factor for development of oral cancer (Zain, 2001; Chen *et al.*, 2004). In India, where such practices were common, oral cancer represented up to 40% of all cancers, compared to just 4% in the UK (Yeole *et al.*, 2003).