

RESEARCH COMMUNICATION

Epidemiological Review of Head and Neck Cancers in Karachi

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Abstract

Head and neck cancers, categories lip, oral cavity, pharynx and larynx are placed amongst the top ten malignancies globally. The cancers have a similar epidemiology, risk factors, morphology, and control measures. The geographical variations in incidence are indicative of the global differences in the prevalence of risk factors. The present study was conducted with the objective of reviewing descriptive epidemiological characteristics, incidence and time trends of head and neck cancers in Karachi (1995-2002). Head and neck cancers accounted for approximately one-fifth (21%) of the cancers in males and about one-tenth (11%) in females in the study period. The age standardized incidence rate (ASR) was 37.1/100,000 in males and 21.7/100,000 in females. In males, oral cavity and larynx were the commonly affected sites, followed by pharynx. In females, oral cavity was the preponderant site. The mean age of the patients was 53.0 years (95% CI 48.0; 58.0). A rising incidence was observed in both genders, more apparent in males. About 30% of oral cancer cases, 28.6% of the nasopharyngeal, 6.3% of the oropharyngeal, and 2.6% of laryngeal cancers occurred in patients 40 years and younger. The age specific incidence rates (ASIR) for oral cancer in males showed a gradual rise from 10 to 64+ years of age, for pharynx from 20 to 64+ and for larynx at 25+. The ASIR for oral cancer in females showed a gradual rise from 14 to 64+ years of age, for pharynx from 20 to 64+, a decade after the oral cancer rise and cancer larynx showed a rise at 25+, a decade and a half after the oral cancer rise. The peak incidence was at 64-69 years for all three cancer sites, in both genders. Pakistan falls into a high risk head and neck cancer geographical zone Presentation is late and treatment is not optimum. Recommendations, therefore for NCCP Pakistan, for short term benefits are selected community-based screening for the high risk population, early diagnosis, better treatment, rehabilitation and palliative care. These measures will improve survival and also contribute to a better quality of life. Primary prevention remains the only strategy for absolute cancer control.

Key Words: Head and neck cancer - Pakistan - cancer control program

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Introduction

Head and neck cancers, ICD-10 (International Classification of Diseases 10th Revision) categories C00-C14 (cancer of the lip, oral cavity and pharynx) and C32 (larynx) are categorized amongst the top ten malignancies globally. Head and neck cancers are grouped together with the justification of similar natural history, epidemiology, risk factors, morphology, and control measures. The major risk factors for the epithelial histological types [Epstein-Barr virus (EBV), Human papillomavirus (HPV), tobacco, arecanut, alcohol, diet, and other environmental and professional exposures] are well-established and common to all (Tumino and Vicario, 2004).

Head and neck cancers mainly comprise squamous cell carcinomas of the upper aerodigestive tract. The majority of these tumours are self-inflicted and preventable as

indulgence in risk factors is avoidable. Tobacco has a distinct carcinogenicity - both as an initiator and promoter in head and neck cancers; alcohol and arecanut are proven carcinogens. The risks associated with smoking, chewing and alcohol consumption are synergistic. Viruses (EBV, HPV) are other important risk factors as are adjuvant carcinogens which act as distinct promotion factors viz. poor dental hygiene for mouth cancer, vocal abuse in laryngeal cancer, Plummer-Vinson's syndrome in post-cricoid cancer and chronic sinusitis in maxillary cancer (Sato, 1987; Dobrossy, 2005).

The geographical variations in incidence and mortality are indicative of the global differences in the prevalence of risk factors. While mouth and tongue cancers are more common in the Indian sub-continent, nasopharyngeal cancer is more common in Hong Kong; pharyngeal cancers are more common in Western Europe and South Central Asia and

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laryngeal cancers in Western Asia, North and South America and the Caribbean (Ferlay et al 2004; Sankaranarayanan et al, 1998).

Squamous cell cancers in the head and neck are mostly associated with visible and symptomatic pre-malignant changes; the lesions are at accessible sites and the transition period is up to 2 decades. Screening could be used to detect both precancerous lesions and early invasive cancers. A recent study demonstrated reduced incidence and mortality from screening for oral cancer in a low resource setting (Sankaranarayanan et al, 2005).

The data for Karachi presented here are derived from the data-base of the Karachi Cancer Registry (KCR) and the Aga Khan University Pathology-based Cancer Surveillance (AKPCS). Karachi Cancer Registry (KCR) established in 1995, as a collaboration of the International Agency for Research on Cancer (IARC) has acquired 11 years stability (1995-2005) for Karachi South (KS), a sample population of Pakistan. The city of Karachi is divided into 5 districts, South, Central, West, East and Malir. Karachi District South has a population of 1,724,915 with 929,394 (54%) males and 795,521 (46%) females, annual growth rate of 1.94% as calculated by the Federal Census Bureau. The population distribution of KS is similar to the population distribution of Pakistan as regards age, gender, and religion. KS has the distinction of being the only district in the country with a representation of all ethnic and socio-economic groups of the country. It is thus a sample population of the country in the absence of other data sources.

The cancer profile (ICD-10 categories) in Karachi South (WHO, 1992; Bhurgri Y, 2004) males is lung (C33-C34 - 11.7%; Age Standardized Incidence Rates- ASR 25.5), oral cavity (C00-C06 - 13.1%; ASR 22.5), larynx (C32 - 6.1%; ASR 11.8), urinary bladder (C67 - 4.8%; ASR 9.9), prostate (C61 - 4.1%; ASR 9.8), lymphoma (C81-85;96 - 7.0%; ASR 9.6), pharynx (C09-14 - 4.3%; ASR 8.2), and colo-rectum (C18-21 - 4.4%; ASR 7.8). In females the commonest cancers are breast (C50 - 34.6%; ASR 69.1), oral cavity (C00-C06 - 8.9%; ASR 8.9), cervix (C53 - 4.1% ASR 8.6), oesophagus (C15 - 3.7%, ASR 8.6), ovary (C56 - 4.2%; ASR 7.8), lymphoma (C81-85;96 - 3.5%; ASR 7.2), gall bladder (C23-C24 - 2.6%; ASR 5.8), and skin (C43-44 - 2.6%; ASR 5.6). The present study was conducted with the objective of reviewing descriptive epidemiological characteristics, incidence and time trends of head and neck cancers in Karachi (1995-2002).

Materials and Methods

Incident head and neck cancers, ICD-10 categories C00-C14 (cancer of the lip, oral cavity and pharynx) and C32 (larynx) registered at the KCR (1995-2004) were reviewed. The cases were categorized by tumour site and the age and sex of the patient. Trends were studied by grouping cases into two periods, period 1 (1995-1997) and period 2 (1998-2002). All morphological types, epithelial, sarcoma and lymphoma were included in the study.

Oral cavity was defined as the area extending from the vermilion border of the lips to a plane between the junction of the hard and soft palate superiorly and the circumvallate papillae of the tongue inferiorly. This region included the buccal mucosa, upper and lower alveolar ridges, floor of the mouth, retromolar trigone, hard palate, and anterior two thirds of the tongue. The posterior two thirds of the tongue was also included in the oral cavity. Pharynx was defined as oropharynx, nasopharynx, and hypopharynx. The hypopharynx was divided into the pyriform sinus (most common site of tumour involvement), posterior pharyngeal wall, and postcricoid region.

The data were classified using ICD-O3 (International Classification of Diseases-Oncology, 3rd edition) and computerized using a customized version of Canreg-4, with internal checks on the validity of entered data (WHO 1990). Manual and computerized validity checks for the cancer data were performed as per recommendations of International Agency for Research on Cancer (IARC) and International Association of Cancer Registries (IACR) (Parkin et al., 1994; Skeet, 1991). This involved factors influencing comparability i.e. classification and coding. All cases whether clinically diagnosed or histologically verified, were included in the study. The residency status of cases was re-ascertained and rechecked. People residing in the specified geographical regions for more than six months were considered residents. Demographical variables recorded were the hospital patient-number, date of incidence, name, age, sex, address, ethnicity, topography, morphology, grading and staging. Tumours were categorized according to the UICC, TNM staging system, to standardize with the staging systems in other parts of the world.

Crude, age-adjusted, and age-specific incidence rates were calculated based on the 1998 census for Karachi South (population of 1,724,915; males 929,394 and females 795,521), annual growth rate 1.94% (Census 1998). The growth rates were based on the inter-census growth-rate and measures for inflow and outflow of population, calculated by the Federal Bureau of Statistics. Standardized incidence rate was calculated with an external reference population, the World population with a given standard-age distribution (Segi, 1960). The methodology applied was direct standardization, using 5-year age groups. The rates given are the annual incidence per 100,000 population, averaged over the number of years for which data are presented. Trends were studied by analyzing the ASR for 2 time periods, 1995-1997 and 1998-2002.

All histologically verified cancers were initially evaluated on Haematoxylin and Eosin (H&E) stained sections and subsequently when required immunohistochemical analysis was performed by employing envision technique. The data were analyzed using Epi-6 incorporated in Canreg-4 and/or SPSS 13.0.

Results

Head and neck cancers accounted for approximately one-

fifth (21%) of the cancers in males and about one-tenth (11%) in females in the study period. The age standardized incidence rate (ASR) was 37.1/100,000 in males and 21.7/100,000 in females. In males, oral cavity and larynx were the commonly affected sites, followed by pharynx. In females, oral cavity was the preponderant site. The ratio oral cavity: pharynx: larynx in Karachi was 2:1:1.5 in males and 5:1:0.5 in females. The male: female ratio was 1.5:3:8 for oral cavity: pharynx: larynx.

The mean age of the patients remained 53.0 years (95% CI 48.0; 58.0) throughout this period (Table 1). Oral cavity was the most commonly affected site. The ASRs per 100,000, period 2 (1st January 1998 to 31st December 2002) in Karachi South were 21.3 in males and 19.3 in females whereas the ASRs per 100,000 for period 1 (1st January 1995 to 31st December 1997) were 14.2 and 14.6 in males and females, respectively. A rising incidence was observed in both genders, more apparent in males. Mucosa cheek was the most common sub-site for oral cancer (55.9%), followed by the tongue (28.4%), palate (6.8%), gum (4.4%), lip (3.1%) and floor of mouth (1.4%). Sub-categories of oral cancer showed a variation in trends over the last decade. Lip cancer (ICD-10 categories C00) in males decreased and the ASR fell from 0.9 to 0.7 per 100,000 from period 1 (1995-1997) to period 2 (1998-2002). The rates remained levelled at 0.4 in females. An increased incidence was observed for tongue (C01-02). The ASR per 100,000 in males increased from 4.2 to 5.3 whereas the rates in females increased from 4.9 to 6.6. The highest increase was observed in cancers of mouth (C03-06). The ASR per 100,000 in males increased from 9.1 during 1995-1997 to 15.3 in 1998-2002; whereas in females the rates increased from 9.3 to 12.3.

The second affected site was larynx. The ASRs per 100,000, in period 2 were 11.8 in males and 1.7 in females whereas the ASRs per 100,000 for period 1 were 8.3 and

Table 1. Mean Ages of Head and Neck Cancers and Frequencies of Histological Confirmation

Body Site	Mean age (95% CI)	HV%
Head and Neck	53.0 (48.0; 58.0)	
Oral Cavity	51.9 (51.1; 52.7)	96.6
Lip	54.4 (51.9; 57.1)	100.0
Cheek	51.9 (51.0; 53.1)	96.6
Tongue	54.0 (52.1; 56.9)	97.6
Pharynx	52.5 (50.7; 54.3)	92.7
Oropharynx	55.2 (51.2; 59.3)	95.8
Nasopharynx	42.8 (38.3; 47.2)	87.1
Hypopharynx	52.0 (48.2; 55.8)	98.1
Larynx	56.6 (55.3; 57.9)	95.5

HV, Histological verification; CI, Confidence Intervals

1.5 in males and females, respectively. A rising incidence was observed in both genders, more apparent in males. The third affected site was pharynx. The ASRs per 100,000, in period 2 were 6.1 in males and 3.1 in females whereas the ASRs per 100,000 for period 1 were 8.3 and 3.6 in males and females, respectively. A decreasing incidence was observed in both genders, more apparent in males (Figure 1).

About 30% of oral cancer cases, 28.6% of the nasopharyngeal, 6.3% of the oropharyngeal, and 2.6% of laryngeal cancers occurred in patients 40 years and younger. Twenty three percent of the oral cancer cases, 1% of nasopharyngeal, 43.5% of oropharyngeal, 35.9% of the hypopharyngeal and 22.3% of the laryngeal cases occurred in patients 65 years and older.

The age specific incidence rates (ASIR) for oral cancer in males showed a gradual rise from 10 to 64+ years of age. The ASIR for pharynx showed a gradual rise from 20 to 64+, a rise being registered a decade after the oral cancer rise and cancer larynx showed a rise at 25+, a decade and a

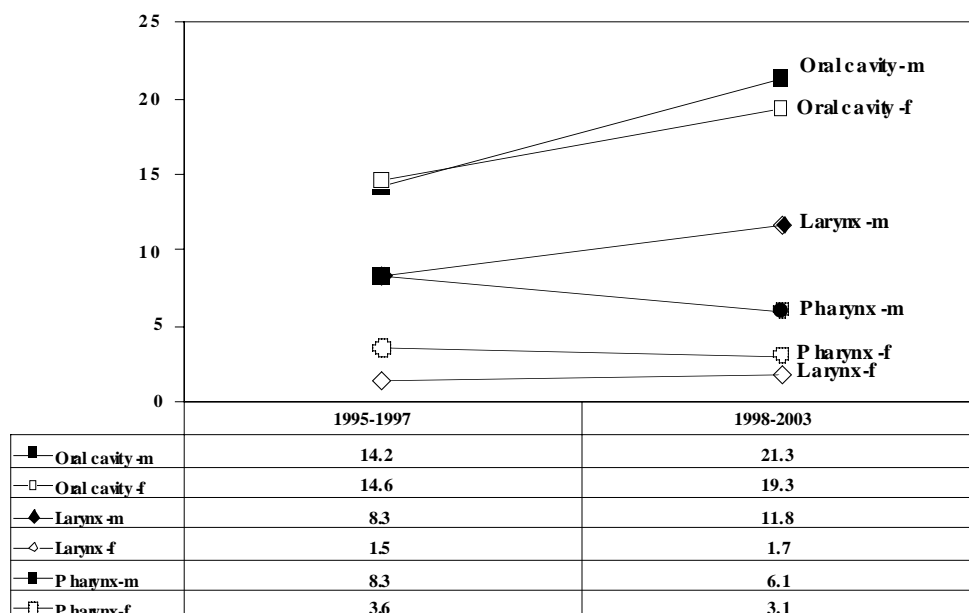


Figure 1. Trends in Incidence Rates for Cancer of the Oral Cavity, Pharynx and Larynx - Males and Females

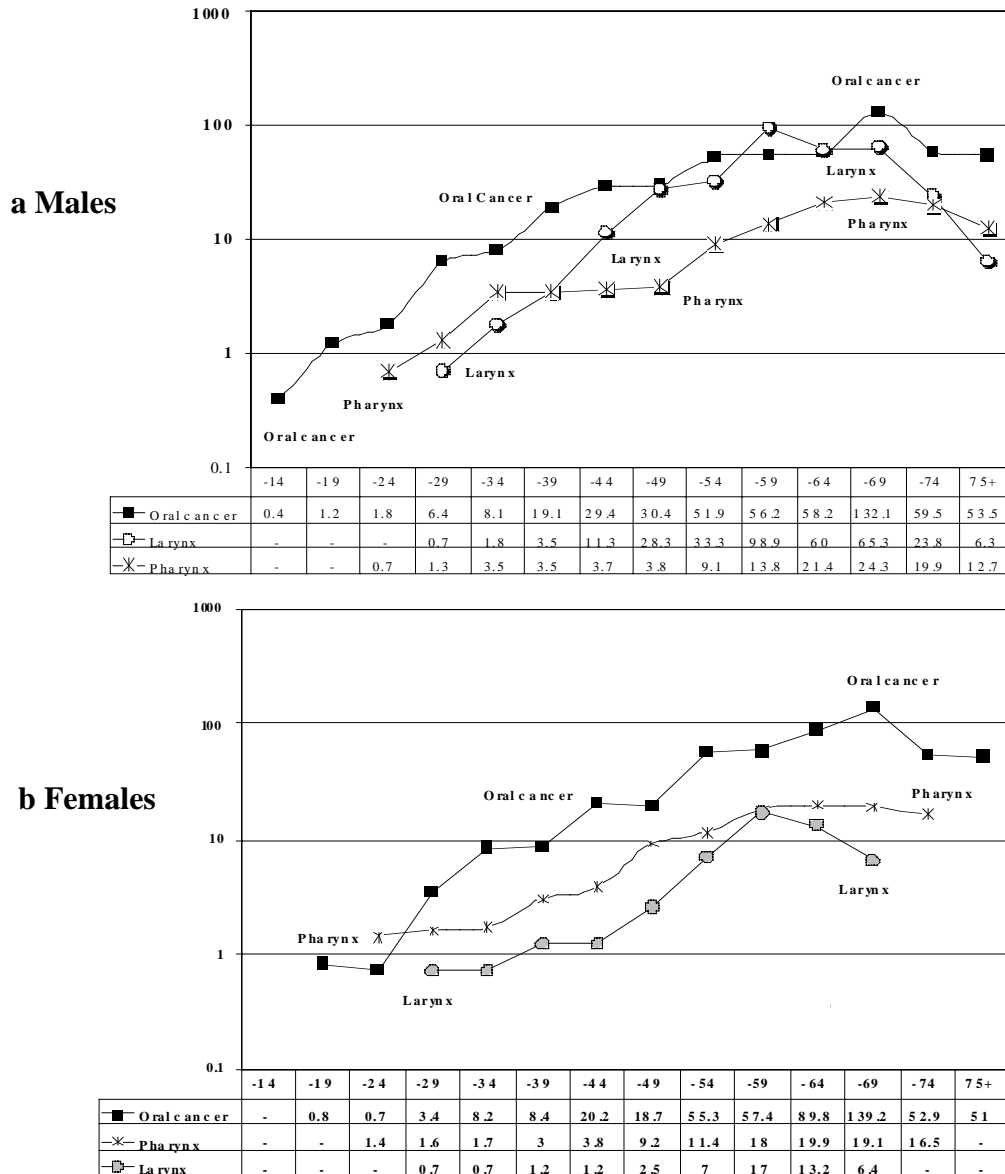


Figure 2. Age-specific Incidence Rates for Cancer of the Oral Cavity, Pharynx and Larynx - Males and Females

half after the oral cancer rise. The peak was at 64-69 years for all three cancer sites, with a subsequent apparent decrease in the risk (Figure 2a).

The age specific incidence rates (ASIR) for oral cancer in females showed a gradual rise from 14 to 64+ years of age. The ASIR for pharynx showed a gradual rise from 20 to 64+, a decade after the oral cancer rise and cancer larynx showed a rise at 25+, a decade and a half after the oral cancer rise. The peak was at 64-69 years for oral cavity and pharynx with a subsequent apparent decrease in the risk (Figure 2b).

Approximately 97% of head and neck cancers were histologically confirmed. The majority of the cancers (47.1%) cases presented as grade II. Two-thirds of the cases were discovered at advanced stages. Of the cancers reported during 1995-2002, 65.0% of the oral cancers had spread to a distant site at the time of diagnosis, stage III or IV. The predominant morphology was squamous cell carcinoma in 96.5% of the cases.

Discussion

Globocan 2002 categorizes geographical cancer regions into 5 ascending zones or grades on a scale of 1 to 5 based on the country-wise annual incidence rates. A global variation in the incidence of head and neck cancers is thus observed. The incidence rates of head and neck cancers in Karachi are comparable to the high risk regions of the world, accounting for approximately 21% of the cancers in males and 11% in females, similar to other reports from this region (Ferlay et al 2004, Yeole et al, 2000; Sankaranarayanan et al 1998; Sanghvi et al 1989). Though other regions in Pakistan, viz. Hyderabad and Larkana also fall into a high risk zone for head and neck cancers, there is a variation in the subcategories. Oral cancer and pharynx fall into the highest risk zone, however for larynx both cities are in zone 4, on a scale of 1- 5 (Bhurgri et al, 2005; 2006). This variation is more marked as we proceed north-west from Karachi, in

the Baluchistan Plateau (Bhurgri et al, 2002), (Table 2).

In the United States, squamous cell carcinoma of the head and neck comprises only about 4% of all malignancies with an estimated incidence rate of 17/100,000 (Ries LAG et al, 2000). Sankaranarayanan R et al in 1998 had reported a high incidence in males (> 30/100,000) in regions of France, Hong Kong, the Indian sub-continent, Central and Eastern Europe, Spain, Italy, Brazil, and among US blacks. High rates (> 10/100,000) were reported in females of the Indian sub-continent, Hong Kong and Philippines. The highest incidence rate reported in males was 63.58/100,000 (France, Bas-Rhin) and in females it was 15.97/100,000 (India, Madras).

The present global scenario indicates the highest reported incidence rates for cancer larynx in males as 15.7 and 15.4/100,000 in Lebanon and Bangladesh respectively and 4.2/100,000 in the females in Iraq. The highest incidence rates for pharynx in males are 15.4 and 16.9/100,000 in France and Hungary with the highest reported rates of 4.8/100,000 in the females in Bangladesh. The highest incidence of oral cancer has been observed in Papua New Guinea (40.9/100,000 M; 26.3 F) and Solomon Islands (34.1/100,000 M; 21.7/100,000 F) (Ferlay et al 2004).

Head and neck cancers usually affect patients above the age of 40 years, especially laryngeal cancer which is generally considered a disease of the elderly, with a peak incidence in the 50s and 60s (Tan et al, 2001). In our study the mean age for all categories of head and neck cancers was above 50. The only exception was the nasopharynx, where the mean age of patients was below 50 years. The peak incidence was in the 64-69 year age group, however approximately a third of oral cancer and nasopharyngeal cancer cases occurred in patients 40 years and younger.

The ratio oral cavity: pharynx: larynx in Karachi was 2:1:1.5 in males and 5:1:0.5 in females. The comparative ratios in this geographical location vary probably reflecting the variation in the mode of use of risk factors like tobacco. The male: female ratio was 1.5:3.0:8.0 for oral cavity: pharynx: larynx. Head and neck cancers are somewhat more common in men than in women (Tan, 2001). The discrepancy in the male-to-female ratio in Karachi is most pronounced in laryngeal tumours; the carcinoma being 8 times more common in men. This ratio has marginally increased in the last 10 years, possibly reflecting a change in the tobacco habits of women in the region.

Most world regions show an increasing incidence of head and neck cancers, with a few exceptions. In Karachi an increasing trend for incidence was observed for all head and neck cancers except lip in men, and pharynx in both genders. The age specific incidence rates for lip cancer in males showed an earlier onset of disease in period two and an associated downward trend in all age groups except 60-64 year age group, whence there was a levelling of rates. There was a decrease in the peak incidence rate. In females an earlier onset and earlier peak was observed for cancer lip. The age specific incidence rates for cancer cheek showed an upward trend in all age groups in both sexes. This increase

Table 2. Head and Neck Cancer Incidences in High Risk South Central Asia, Based on Globocan 2002 Ascending Scale of 1 to 5

Region	Globocan 2002 Ascending Scale of 1-5				
Oral Cavity; male	<2.6*	<3.9*	<5.9*	<8.6*	<40.9*
KS 95-97; 98-02	†	†	†	†	14.2;21.3
Larkana 2000-02	†	†	†	†	12.0
Hyderabad 1998-02	†	†	†	†	11.8
Quetta 1998-99	†	†	†	3.8	†
India	†	†	†	†	12.8
Sri Lanka	†	†	†	†	24.5
Bangladesh	†	†	†	†	13.4
Oral Cavity F	<1.3*	<1.8*	<2.4*	<3.3*	<26.3*
KS 95-97; 98-02	†	†	†	†	14.6;19.3
Larkana 2000-02	†	†	†	†	12.6
Hyderabad 1998-02	†	†	†	†	11.5
Quetta 1998-99	†	†	†	2.5	†
India	†	†	†	†	7.5
Sri Lanka	†	†	†	†	14.7
Bangladesh	†	†	†	†	16.8
Larynx; male	<2.3*	<3.5*	<5.3*	<8.1*	<15.7*
KS 95-97; 98-02	†	†	†	†	8.3;11.8
Hyderabad 1998-02	†	†	†	3.2	†
Larkana 2000-02	†	†	†	6.1	†
Quetta 1998-99	0.9	†	†	†	†
India	†	†	†	6.2	†
Sri Lanka	†	†	†	6.8	†
Bangladesh	†	†	†	†	15.4
Larynx; female	<0.3*	<0.5*	<0.7*	<1.0*	<4.2*
KS 95-97; 98-02	†	†	†	†	1.5;1.7
Hyderabad 1998-02	†	†	†	1.0	†
Larkana 2000-02	†	†	†	0.8	†
Quetta 1998-99	0.3	†	†	†	†
India	†	†	†	0.8	†
Sri Lanka	†	†	†	†	1.5
Bangladesh	†	†	†	†	3.3
Pharynx; male	<0.9*	<1.6*	<2.2*	<4.6*	<16.9*
KS 95-97; 98-02	†	†	†	†	8.3;6.1
Larkana 2000-02	†	†	†	†	6.6
Hyderabad 1998-02	†	†	†	4.2	†
Quetta 1998-99	†	1.0	†	†	†
India	†	†	†	†	9.6
Sri Lanka	†	†	†	†	6.9
Bangladesh	†	†	†	†	12.5
Pharynx; female	<0.2*	<0.4*	<0.6*	<0.9*	<4.8*
KS 95-97; 98-02	†	†	†	†	3.6;3.1
Larkana 2000-02	†	†	†	†	3.2
Hyderabad 1998-02	†	†	†	†	1.6
Quetta 1998-99	†	†	†	†	1.7
India	†	†	†	†	1.8
Sri Lanka	†	†	†	†	2.6
Bangladesh	†	†	†	†	4.8

KS, Karachi South

was dramatic in the younger age groups (Bhurgri, 2005; Bhurgri et al, 2003). The age specific rates for oral cancer for all age groups were higher than for cancer larynx and pharynx. The apparent decrease in the risk in the 65+ age group is a probable cohort effect.

The overall trends of head and neck cancers are a reflection of underlying prevalence of risk factors. Whilst the incidence rates show a declining trend in both sexes in India, Hong Kong, Brazil and US whites, an increasing trend is observed in most other populations, particularly in Central and Eastern Europe, Scandinavia, Canada, Japan and Australia (Sankaranarayanan et al, 1998). The Italian Network of Cancer Registries (pool AIRT) during the period 1986-1997, showed diverging trends between sexes; rates decreased significantly among males and increased among females. Decreasing trends were observed for pharynx, statistically significant only among males. Larynx cancers showed a significant decreasing trend among males; trends were stable among females (Tumino and Vicario, 2004).

In Karachi mucosa cheek was the most common site for oral cancer (55.9%), followed by the tongue (28.4%), palate (6.8%), gum (4.4%), lip (3.1%) and floor of mouth (1.4%). According to the National Cancer Institute's Surveillance, Epidemiology, and Ends Results (SEER) program, 30 percent of oral cancers originate in the tongue, 17% in the lip, and 14% in the floor of the mouth (NCI, 2001). The difference in the subsite of involvement in the two geographical areas is probably indicative of the difference in risk factors. Though there is a possibility that there could be some degree of misclassification by subsites, giving the close anatomical proximity of component head and neck cancer topographic sites..

Head and neck cancers if detected in early stages are highly curable, unfortunately two thirds of the cancers reported during 1995-2002 were a stage III or IV disease, having spread to a distant site at the time of diagnosis. Diagnosis relies on patient presentation and pickup by physician. Almost all (80%) the patients in Karachi loose precious time (up to 3 years) between first presentation to clinician and final confirmation. This delay contributes to the late stage of diagnosis and indicates the necessity of training for the physicians and other health workers working at community level.

Conclusion

Pakistan falls into a high risk Head and Neck Cancer geographical zone Presentation is late and treatment is not optimum. Recommendations, therefore for NCCP Pakistan, for short term benefits are selected community-based screening for the high risk population, early diagnosis, better treatment, rehabilitation and palliative care. These measures will improve survival and also contribute to a better quality of life. Primary prevention remains the only strategy for absolute cancer control.

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