RESEARCH COMMUNICATION

Cancer Profile of Larkana, Pakistan (2000-2002)

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Abstract

   This present study was conducted with the objective of providing the cancer profile of Larkana, the fourth largest city of Sindh, Province. The study included two sets of patients. The first set included the incident cancer cases, residents of Larkana, who reached Karachi for diagnosis or treatment. The second set consisted of the incident cancer cases registered at the Aga Khan University (AKU) Pathology collection points at Larkana during 1st January 2000 to 31st December 2002. The age-standardized rates (ASR) for cancer (all sites) were 134.2/100,000 in males and 110.3/100,000 in females. The most common malignancies in males were lymphoma, oral cavity, prostate, liver, and urinary bladder. Cancers in females were breast, oral cavity, lymphoma, skin and thyroid. Tobacco-associated cancers accounted for approximately 35.0% of the tumors in males and 18.6% in females. The gender ratio was 1.5, the mean age of cancer all sites was 45.5 years (95% CI 34.6; 56.4) in males and 42.9 years (95% CI 33.6; 52.2) in females. This is the first attempt to determine the cancer incidence pattern of Larkana and should serve as a guideline for estimation of the cancer burden of Pakistan and the cancer control program of the country. The data must be interpreted with care, as they are largely pathology-based with approximately 15-30% population-wise under-registration. However, the chances of selective collection bias were minimized as the AKU pathology specimens were collected from 2 centers within the city, Each collection centre provided diagnostic service to several health centres giving wide population coverage, thus ensuring adequate sampling from the entire city.

Key Words: Cancer registration - Larkana - Pakistan

Introduction

   To combat the cancer epidemic, cost effectively the assessment of the geographical cancer burden and the variations in different regions on the basis of risk factors is essential. This risk assessment is available for the developed countries but the precise burden of cancer and risk assessment statistics are scarce for the developing countries. Pakistan is a developing country, which falls into the low to medium resource category by WHO classification (World Health Report, 2005). The only cancer incidence data available for any region of Pakistan is from Karachi, as calculated by the Karachi Cancer Registry (KCR), established in 1995. The registry was developed with the perspective of measuring the cancer burden through a sample population of the country. KCR has acquired 11 years stability (1995-2005) for the data of Karachi South (KS), the sample population of Pakistan (Bhurgri et al., 2000; 2002a).

   The Aga Khan University Cancer Surveillance for Pakistan (ACSP), was established in 2000 at the Aga Khan University Pathology-based Cancer Registry (APCR), and covers a large geographical area and population of Pakistan, through 84 centers. This coverage is likely to increase at the rate of a minimum of 10 new centers annually in the future. This data has been of immense value in determining the geographical variation of malignancies in Pakistan and as a strong prop for KCR. APCR is an associate member of the IACR (Bhurgri et al., 2002b).

   KCR has stable incidence rates for KS (1995-2004) and with the help of ACSP has calculated the incidence of Karachi Division (1998-2002), population of 9,802,134 [53% males (M) and 47% females (F)] annual growth rate 3.52; Quetta (1998-1999) population 759,245 [56% males (M) and 44% females (F)], annual growth rate 4.13 and Hyderabad urban population of 2,840,653 (52.2% M, 47.8% F) annual growth rate 1.13 (Census 1998, Bhurgri et al., 2002 c & d; 2005).

   Larkana is a growing city in the Northwest of Sindh Province; the fourth largest city of the Province. The name Larkana is taken from the Caste of the people who live in the city, "Lark". In the year 2000, August, Larkana celebrated

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it's 100 hundred years of existence. Larkana has fertile land that cultivates all kind of fruits and vegetables, including potatoes, melons, olives, oranges, peas, carrots, cucumber, and mangoes. Sindhis constitute 83%, Mohajirs 6%, and Balochis and Siraikis, 6%, whilst the rest are different ethnical inhabitants. Many casts dwell in the City Abbasi, Abra, Bhurgri, Bhutto, Bugti, Burdi, Chandio, Jatoi, Leghari, Sama, Sheikh, Soomra etc. Sindhi is the central language of almost all the people. Siraikis is also widely spoken, which is similar to the Sindhi language. Larkana it is at a distance of approximately 450-km from Karachi. This present study was conducted with the objective of providing the cancer profile of Larkana.

Materials and Methods

The study includes two sets of patients. Firstly the incident cancer cases, residents of Larkana who reached Karachi for treatment and were registered at the Karachi Cancer Registry. Secondly the incident cancer cases registered at the AKU Pathology collection points at Larkana and subsequently registered at APCR, during 1st January 2000 to 31st December 2002. The pathology department of the AKU has 2 centers in Larkana, which cater to the diagnostic pathology needs of the city, especially onco-pathology.

The data of 'AKU Pathology Department', included for this paper was diagnosed on the basis of histopathology, fine needle aspiration cytology, fine needle aspiration biopsy and hematology during the 3 year period. The demographic details of the registered pathology data were precise and complete. Items such as age, sex, name, address, telephone numbers and nature of surgery were well recorded. At the APCR both the in-patients and the out-patients were given a specific cancer registration number and information updated with every revisit. It was thus possible to recognize duplicate examinations of the same patient. The variables that were recorded were the hospital patient-number date of incidence, name, age, sex, address, topography, morphology, grading and staging. This required a well-trained staff available at all the collection points of this University lab in Larkana and also of the registration staff at the main lab in Karachi. Awareness of the legal and academic requirements of accuracy of demographic data was a part of the training of the collection staff. Validity checks and random retrace of cases was conducted for follow-up and for confirmation of the information recorded.

Internal and external quality checks were used for diagnostic pathology. External quality assurances for diagnostic pathology were maintained by the College of American Pathologists (CAP) surveys. Internal quality control and standardization of the diagnosed data was maintained by using prompt and adequate fixation, grossing as per standard protocol and using histochemical stains, immunohistochemical techniques and biological markers as and when required. ISO 9002 certified the clinical pathology lab in 1999. Consensus diagnosis of all doubtful cases at the daily departmental consultation conferences improved the quality of diagnosed data. Immunohistochemistry was used for malignancies, which necessitated cellular typing and sub-typing.

The cancer data of KCR and APCR for cancer registration purpose were classified using ICD-O2 (International Classification of Diseases-Oncology, 2nd edition) and computerized using a customized version of Canreg-3 (WHO, 1990). Manual and computerized validity checks for all 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). This involved factors influencing comparability i.e. classification and coding. Tumors were categorized according to the UICC, TNM staging system for global comparability.

Incidence rates were calculated based on the 1998 census for Larkana, urban population of 552,509 (51.8% M, 48.2% F) annual growth rate 4.635. 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 (Census 1998). The data were analyzed using SPSS 13.0.

Results

The age-standardized rates (ASR) for cancer (all sites), 2000 to 2002 in Larkana were 134.2/100,000 in males and 110.3/100,000 in females. The most common malignancies (ASR per 100,000) in males were lymphoma (15.5), oral cavity (12.0), prostate (11.1), liver (10.5), urinary bladder (9.0), skin (8.7), lung (6.6), pharynx (6.6), colo-rectum (6.3), and connective tissue (5.4). The cancers in females (ASR per 100,000) were breast (20.6), oral cavity (12.6), lymphoma (8.4), skin (6.6), thyroid (6.4), stomach (4.8), ovary (4.4), gall bladder (3.2), pharynx (3.2) and colo-rectum (3.2) – Figures 1 and 2. Tobacco-associated cancers were responsible for approximately 35.0% of the tumors in males and 18.6% in females (Table 1).

Males comprised 59.1%, and females 40.9% of the cases. The mean age of cancer all sites was 45.5 years (95% CI 34.6; 56.4) in males and 42.9 years (95% CI 33.6; 52.2) in females. The minimum age was <1 year for both genders (childhood cancers) and maximum was 98 years for males and 95 years for females. A higher risk in males was observed in tobacco associated cancers and lymphoma (Table 1). Histological confirmation remained 95.0%, with 63.8% presenting in grade II or I; 59.4% presenting as stage III and IV. Information on grade and stage of malignancy was available in 60% of the cases respectively.

Oral cancer accounted for 12.0% of all cancer cases in

Table 1. Cancer Incidence in Larkana (2000-02)

	Male	Female	Male:Female	ICD (10th)
Oral Cavity	12.0	12.6	1.0	C00-08
Pharynx	6.6	3.2	2.1	C09-14
Esophagus	2.0	2.2	0.9	C15
Stomach	2.6	4.8	0.5	C16
S.Intestine	0.2	1.2	0.2	C17
Colo-rectum	6.3	3.2	2.0	C18-21
Liver	10.5	2.0	5.3	C22
Gall bladder	0.6	3.0	0.2	C23-24
Pancreas	0.5	0.1	5.0	C25
Nose, sinuses etc.	1.1	0.8	1.4	C30-31
Larynx		6.1	0.8	5.9
C32				
Bronchus, lung	6.6	0.4	16.5	C33-38
Bone	5.1	1.8	2.8	C40-41
C. tissue	5.4	2.6	2.1	C47;49
Melanoma skin	0.4	0.8	0.5	C43
Other Skin	8.3	5.8	1.4	C44
Breast	3.0	20.6		C50
Uterus	-	2.2	-	C54-55
Cervix	-	2.2	-	C53
Placenta	-	1.4	-	C58
Ovary	-	4.4	-	C56
Female genital, other	-	1.2	-	C51-52;57
Prostate	11.1	-	-	C61
Testis	1.0	-	-	C62
Penis	0.1	-	-	C60
Bladder	9.0	2.8	3.2	C67
Kidney	1.2	1.0	2.0	C64-66;68
Eye	0.6	0.6	1.0	C69
Brain, N. system	3.0	2.0	1.5	C70-72
Thyroid	1.7	6.4	0.3	C73
Lymphoma	15.5	8.4	1.9	C81-85;96
Multiple myeloma	0.4	1.4	0.3	C88;90
Leukemia	2.0	1.8	1.1	C91-95
Unspecified	11.3	8.6	1.3	
All sites	134.2	110.3	1.2	

the males and 12.6% in the females. In males the most common site was the mucosa cheek (66.7%), followed by tongue (22.2%), and lip (11.1%). The distribution in females was mucosa cheek (79.0%), followed by tongue (14.0%) and lip (7.0%). The minimum age at diagnosis was 30 years in both genders. About 17% of the oral cancer cases occurred in patients 40 years and younger and 26% occurred in patients 65 years and older.

The common childhood cancers were Hodgkins Disease, non-Hodgkins lymphoma, retinoblastoma, soft tissue and bone sarcomas, endocrine tumors and liver. The male-female gender ratio in childhood cases was 4.

Discussion

Larkana is the northern-most of the big cities of the province of Sindh in Pakistan. On the whole the patterns of malignancy in Larkana are similar to the patterns in Karachi, with a few exceptions. The age-standardized rates (ASR) for cancer (all sites), are low in comparison to the incidence rates of Karachi South. Though the AKU pathology has good oncopathology coverage in Larkana, nonetheless there is approximate 15-20% incompleteness in the data, all data sources not being utilized. We are also missing the malignancies in Larkana which were not diagnosed at the AKU pathology department; though a large number of these cases either came to Karachi for diagnosis, treatment or simply a second opinion.

The registry data at KCR and APCR had a reasonable precision of recorded addresses. However other than this, the clinical and pathology data in Larkana was not utilized as records were either not preserved or preserved without addresses thus the residency status could not be established. The death registry data was also not informative as it was not cause specific. As with most developing country cancer registration we may also be missing cases with advanced malignancies who may not be subjected to intense diagnostic procedures, older patients or females who may not be entering the health sector and the socio-economically deprived who may not have access to medical care. The percentage of cases with microscopic verification is high and similar to the values in the developed countries reflecting the predominantly pathology-based origin of the data. The cases coming to Karachi for treatment and reported to KCR have a high microscopic verification due to insistence of clinicians establishing verification prior to initiation of therapy.

Larkana like Karachi falls into the Asian oral cancer zone, which includes a part of Pakistan adjacent to India. Cancer oral cavity (ICD C00-06) is the second-most common malignancy in both genders. This pattern is also observed in Karachi and reflects probable exposure to similar risk factors. The high oral mucosa and tongue lesions lend support to oncogenesis associated with the chewing of areca nut, betel quid chewing, pan masala, and gutka in the population. In Pakistan generally, alcohol is a notable omission as a risk factor. The higher rates for oral cancer in Karachi are indicative of a similarity of chewing-habits in the Mohajir (Indian immigrant) population in Karachi and their country of origin i.e. India (Jafarey, 1994; Alam, 1998; IARC monograph 85, Merchant, 1998; and Sankaranarayanan, 1998; 1990). By and large, chewing is not a culturally prevalent habit in Pakistan. The oral cancer risk seems slightly lower in Larkana in comparision; the proportion of Mohajirs in this population is far less then in Karachi.

Hypopharynx was the most common site for cancers in the pharynx, a pattern observed in Karachi and other regions of the subcontinent (Bhurgri et al., 2000). The incidence rates of cancer lung, larynx and esophagus are lower than the rates in Karachi and may represent either a lower prevalence of risk factors such as tobacco smoking or under-registration of these cancers; not all cases necessarily biopsied. The age-standardised incidence rate for lung cancer was sixteen times higher risk as compared with the females, the ratio being one of the highest in the world region. It may indicate a lower risk in females or an under-registration in a conservative society, where women are less likely to enter

the health-care system.

The incidence of stomach cancer is low despite a high prevalence of *Helicobacter pylori* infection in the population. The pattern is similar to Karachi and other regions of the subcontinent, indicating a role of dietary protective factors (Kazi et al., 1990). The incidence of cancer gall bladder is high in females, the latter comparable to the high risk regions of the world.

Breast cancer is the most frequent cancer in the females. This pattern is observed in almost all regions of Pakistan though the ASR is higher in Karachi South, a more westernized region of the country. The only exception is Quetta which reports esophageal cancer as the most frequent cancer in females followed by breast as the second-most common cancer (Bhurgri et al., 2003). Reproductive factors cannot be considered risk factors in Pakistan, as early marriages, multiple births and prolonged breast-feeding are the prevalent cultural norm. Early menarche, late menopause and thus the prolonged effect of reproductive hormones could be other possible risk factors along with dietary factors and obesity. The predominant histological type was duct cell carcinoma.

Malignancies of the female genital tract i.e. cervix, ovary and uterus (body) comprised 10.9% of the total cancers in the females. The rates for cancer cervix are low compared to the Asian region, especially India but similar to the Western Asian Muslim countries. Cancer of the ovary is the seventh most common malignancy rated at number three in Karachi South. Germ cell tumours were the dominant morphology in the younger age group. The age-specific curves show a gradual increase in risk uptil the 7th decade, for uterus and ovary and the 8th decade for cervix. The apparent lower risk for prostate cancer may be an indicator of 'missing cancers' diagnosed on the basis of clinical investigations. The lower life expectancy in Pakistan and also the lack of post-mortems substantially contribute to the low age-standardised incidence rates for prostate in comparison to the developed countries.

'It is an acceptable fact that information on cancers obtained from the registers or databases of selected medical institutions, represent only a proportion of all those occurring in the population. The data may be biased in terms of tumor type, sex, age, socio-economic group, etc, depending on the nature of the institution(s) and the treatment facilities available' (Parkin, 1986). The data of the AKU pathology are collected from multiple centers in the city, dispersed at distances which allow adequate sampling from the entire city and chances of selective collection bias are thereby minimized.

Conclusions drawn from this database must naturally be interpreted with care. The slight preponderance of lymphomas may indicate an internationally accepted over representation of easily accessible sites in pathology based-data and the pattern of a referral center for lymphomas. However, this may be a true higher risk, because a pathology-based bias would also be reflected in the females, but that was in fact not observed.

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