RESEARCH COMMUNICATION

Time Trends in the Incidence of Cancer Cervix in Karachi South, 1995-2002

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Abstract

Introduction: The objective of the study was to determine the trends of cancer cervix in Karachi South during an eight (1995-2002) year period. Methodology: Cancer cervix cases recorded at Karachi Cancer Registry during 1st January 1995 to 31st December 2002 were analyzed. Trends were studied by analyzing the age standardized incidence rates (ASR)s in 2 time periods, 1995-97 and 1998-2002. Results: Cancer cervix ranked sixth in the 1995-97 period the age standardized incidence rate (ASR) world and crude incidence rate (CIR) per 100,000 were 6.81 and 3.22. It reached the fifth ranking in the 1998-2002 period with an ASR and CIR of 7.5 and 4.0 per 100,000. Thus between 1995 and 2002, the incidence of cervical cancer registered an approximate 10% increase. The mean age of the cancer cases was 53.27 years (SD 11.6; 95% CI 50.58, 55.96; range 32-85 years) and 50.68 years (SD 11.7; 95% CI 48.8, 52.5; range 51 years) in period 1 and 2 respectively. The morphological components of squamous cell carcinoma and adenocarcinoma remained stable during this period, though a marginally higher component and increasing incidence of adenocarcinoma was observed throughout. A negligible down staging was observed in the 1998-2002 period. Localized malignancy was observed in 30.8% in period 2 as compared to 25.7% in period 1 and the component of carcinoma in situ increased from 0% percent in period 1 to 1.3% in the second period. Despite this two thirds of the cases still presented with a regional or distant spread of disease. Conclusion: Pakistan at present falls into a low risk cancer cervix region. The cause of concern is the steadily increasing incidence especially in the younger birth cohorts, the advanced disease at presentation; insignificant in-situ cancers and no preventive intervention or awareness practices in place.

Key Words: Cancer cervix - time trends - Karachi, Pakistan

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Introduction

Cancer cervix uteri is globally reported as the second commonest malignancy affecting women (Jemal et al., 2002). Worldwide, about 450,000 women are diagnosed with cervical cancer each year which kills 200,000 annually (Pisani et al., 1999). Almost 80% of these deaths occur in developing countries, where cervical cancer is the leading cause of cancer mortality in women (Ghafoor et al., 2002).

During the two and a half decade period (1973 to 1997) the incidence rates of cervical cancer decreased in almost all parts of the developed world. In contrast the incidence rates for cancer cervix increased in the less-developed countries and are currently almost two-fold higher in comparison. The incidence is highest in Africa, India and Central/South America (approximately 29 per 100,000 person years -PY) and lowest in Oceania, North America and most Muslim countries (approximately 7.5 per 100,000 PY). Mortality rates also vary more than 10-fold across continents, therefore the ratio of mortality and incidence rate (MR:IR) ranges from 0.27 in Oceania to 0.79 in Africa (Kamangar et al., 2006).

Massive Pap screening in the United States was credited with bringing cervical cancer to number 10 in the causes of cancer death from being the leading cause in 1941 (Creasman et al., 1998). Reports from Europe claim that the introduction of cervical screening programs to unscreened populations reduced cervical cancer rates by 60-90% within three years (McCrory et al., 1999).

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When cervical cancer trends in North America and Europe were correlated significant reductions in the incidence of invasive cervical cancer and a 20% to 60% reduction in cervical cancer mortality was reported (McCrory et al., 1999).

Post 1997 the below 50 years cohort in North America, Europe and Australia have shown an increasing trend. This cohort effect could reflect the use of new diagnostic techniques, such as human papillomavirus (HPV) testing and cervicography. Another factor potentially affecting incidence trends is the increase in rates of adenocarcinomas and adenosquamous carcinomas (Vizcaino et al., 1998).

The reported incidence of cervical cancer in Karachi South (1995-97) reflects a low risk population with a late presentation. The age standardized incidence rate (ASR) world and crude incidence rate CIR) per 100,000 for cancer cervix have been reported as 6.81 (5.2, 8.43) and 3.22 (2.49 to 3.96) for the years 1995-97. Cancer cervix accounted for approximately 3.6% of all cancers in females and was the sixth commonest malignancy in women (Bhurgri et al., 2007a; 2007b).

The objective of the study was to determine the time trends in cancer cervix incidence in Karachi South during an eight (1995-2002) year period.

Materials and Methods

Epidemiological data of incident cancer cervix cases, ICD-10 category C53 registered at Karachi Cancer Registry (KCR) for Karachi South, during 1st January 1995 to 31st December 2002 were reviewed. Trends were studied by grouping cases into two periods: period 1 (1995-1997) and period 2 (1998-2002). Results for period 1 have been published (Bhurgri Y et al, 2007). Results for period 2 are given in the section on results.

The study included clinically diagnosed and microscopically verified cancer cervix cases. All surgical specimens were initially evaluated on Hematoxylin and Eosin (H&E) stained sections. Special stains were selectively used, whenever required. The reported epidemiological cancer data were rechecked and residency status re-ascertained. 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 (TNM).

The data were classified using ICD-O3 (International Classification of Diseases-Oncology, 3rd edition) and computerized using a customized version of CANREG-4 software. This software includes facilities for the detection of duplicate registrations and for performing internal checks on the validity of the entered data. 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). This involved factors influencing comparability i.e. classification and coding.

Crude, age-standardized, and age-specific incidence rates (CIR, ASR, ASIR) were calculated for cancer cervix. Incidence tables were based on ICD-10 (WHO, 1992). The person-years of female population at risk by 5-year age-groups were estimated with the mid 2000 population, estimates based on the 1998 census, copy obtained from the Sindh Bureau of Statistics. The estimated population of females was 794, 920 assuming an annual growth rate of 1.94%. 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 standardized rate is the incidence rate that, theoretically, would have been observed if the population had a standard age distribution. 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'. Data were analyzed using SPSS 16.0.

Results

A total of 233 cases of cancer cervix, ICD-10 category C53 were registered at the Karachi Cancer Registry, for Karachi South, during an 8 year period, 1st January 1995 to 31st December 2002. Seventy four cases were recorded in period 1 (1995-97) and 159 cases in period 2 (1998-2002). The comparative distribution by age, religion, ethnicity, education, occupation, marital status and morphology for both periods is given in Table 1.The age standardized (ASR) and crude incidence rates (CIR) per 100,000 were 6.81 and 3.22 for period 1; 7.5 and 4.0 per 100,000 for period 2. Cancer cervix accounted for approximately 3.6% and 3.9% of all cancers in females in period 1 and 2 respectively.

In the second period the age-specific incidence curves (ASIR) showed a gradual increase in from the third up till the sixth decade, followed by an actual apparent decrease in risk after 70 years of age (Figure 1). In the first period the ASIRs had shown an increase from the fourth up till the sixth decade, followed by an actual apparent decrease in risk after 70 years of age. The peak incidence was observed in the 55-59 year age group in both periods.

The majority of the cases presented as moderately differentiated or grade 2 lesions (72 cases; 45.3%). Well differentiated (grade 1) and poorly differentiated (grade 3) malignancies contributed 40 (25.2%) and 37 (23.2%) of the cases respectively. The tumor grade was not known for 10 (6.3%) cases.

Discussion

Cancer cervix in the last decade in Karachi South has remained a malignancy with a low incidence. The cause of concern is the steadily increasing incidence especially in the younger birth cohorts, the advanced disease at presentation, insignificant in-situ cancers, the relatively high adenocarcinoma and no cancer screening or awareness practices in place.

Pakistan is one of the few large populated countries

Table 1. Frequency of Cancer Cervix Cases with Reference to Morphology, Religion, Education, Ethnicity, Marital Status, Occupation & Stage at Presentation

	1995-1997	1998-2002
Age standardized incidence rate	6.8	7.5
Crude incidence rate	3.2	4.0
Relative frequency	3.6	3.9
Mean age (years)	53.3	50.7
Morphology (%)		
Squamous cell carcinoma	86.5	85.4
Adenocarcinoma	10.9	10.8
Adenosquamous	2.6	0.6
Unspecified	-	3.2
Religion (%)		
Muslims	90.5	94.3
Christians	8.1	2.5
Hindus	1.4	3.1
Education (%)		
Illiterates	55.4	63.5
Graduates	19.0	22.0
Ethnicity (%)		
Urdu speaking Mohajirs	20.3	30.1
Punjabis	17.6	19.5
Sindhis	10.8	10.1
Baluchs	8.1	8.2
Memon Mohajirs	8.1	6.3
Pathans	5.4	10.7
Gujrati speaking Mohajirs	4.1	7.5
Afghan migrants	2.7	3.8
Unknown	22.7	3.8
Marital status (%)		
Married	86.5	91.2
Unmarried	2.7	1.3
Widows	10.8	6.3
Occupation (%)		
Housewives/unskilled workers	97.2	97.5
Professionals	2.8	2.5
Stage (%)		
In situ	-	1.3
Localized	25.7	30.8
Regional spread	58.1	59.7
Distant disease	8.1	6.3
Unknown	8.1	1.9

without any preventive intervention for cancer cervix, thus the increasing incidence and the late presentation. Most developed countries in the world currently show a low incidence of cervical cancer attributed to extensive cancer screening practices (Kamangar F et al, 2006). Developing countries in high risk regions and less developed areas in the developed countries, which had previously shown alarm, but implemented cervical screening are also showing a decreasing trend (Yeole BB, 2008; Day GE et al, 2007).

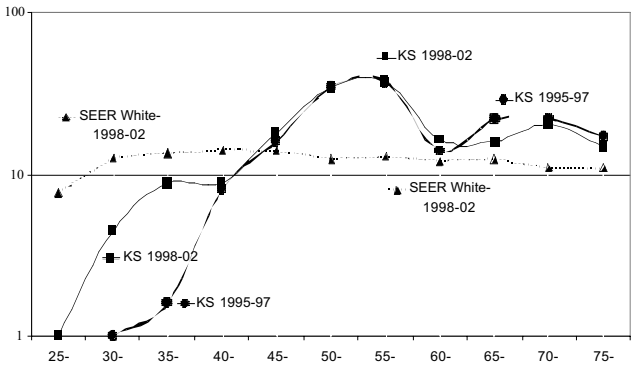

Figure 1. Age-standardized Cervix Cancer Incidence Rates in Karachi South (1995-1997, 1998-2002) in Comparison with SEER Data

The age specific curves in Karachi South for both periods show a developing country pattern with lower rates in the younger women, a sharp increase after 40 years, peak between 50-55 years, followed by an apparent decrease in risk, which can be interpreted as a cohort effect. Age-specific incidence rates for cancer cervix generally reveal unique patterns, being higher in younger individuals in the more-developed countries, but plateau after the age of 40 years, a phenomenon not seen in the less developed countries. In contrast the less-developed countries show lower rates at younger ages which subsequently increase after age 40 years to exceed those in more-developed countries. The pattern in the more-developed countries may in part be attributed to screening practices (Kamangar F et al, 2006). These effects are apparent in figures 1 where the Karachi South and SEER white ASIRs are compared.

In Karachi, the highest registered increase in the incidence of cancer cervix was observed in the younger age group (<39 years). The rates remained stable in the older age group (figure 1). The incidence rates in the younger females are only marginally lower then the rates of contemporary females in the developed countries like US. As these are younger birth cohorts, age, this pattern should translate into a substantial increase in the incidence and occurrence of cervical cancer in Karachi and probably Pakistan. In the absence of preventive intervention the cancer cervix rates in the future may parallel those in the high risk zones.

Late presentation and advanced disease remain the hallmark of cancers in Karachi and cancer cervix is no exception. In both period 1 and 2 approximately two third the cancers had spread regionally or to a distant site at the time of diagnosis, indicating that the last decade saw virtually no cancer cervix awareness in the country. Most women with cervical cancer in developing countries present with advanced disease, resulting in low cure rates. This reflects the poor health structure and the lack of availability and accessibility of cancer control measures (Kamangar et al., 2006; Patro and Nongkynrih, 2007).

In the last decade there has been no increase in the in-situ cancers in Karachi, which remains a grim reality facing the health providers. In developed countries ever since the late 1980s there has been an increase in the incidence rates of carcinoma in situ for women under 30. For women aged 30-34 there was an increase since 1992, though there have been no apparent increases for women over 34 (Quinn et al., 1999; 2001). The pattern of cervical cancer in Karachi and almost all Muslim countries appears linked to the comparatively more conservative life-style pattern and a lesser exposure to risk factors, which has kept this large block somewhat safe. The cause of alarm is the increasing incidence in the younger birth cohorts which may transform this region into a higher risk zone in the future.

Almost all cervical cancer cases are caused by one of

the 15 types of oncogenic human papillomavirus (HPV), with HPV subtypes 16 and 18, accounting for the majority of cervical cancer cases (Schiffman and Brinton, 1988; Bosch and de Sanjose, 2003; Munoz et al, 2003). Other associated risk factors include low socioeconomic status (Fasal et al, 1981; Brinton et al, 1987), smoking (Hellberg and Stendahl, 2005), multiple sexual partners, promiscuous sexual partners, sexual relations at a young age (Schiffman and Brinton, 1988) and oral contraceptive use (Hellberg and Stendahl , 2005; Castellsague and Munoz, 2003). The presence of HPV infection is a *sine qua non* in cervical carcinogenesis, and most other factors mediate their effect via exposure to HPV or by affecting susceptibility to the carcinogenic effects of HPV.

The threat of cancer cervix can only be averted by implementation of stringent cervical cancer control measures, population-wide HPV vaccination and health education. The introduction of HPV vaccine at this time may be strongly recommended to avoid this disaster. Two HPV vaccines are currently on the market, Gardasil (Merck & Co.) and Cervarix (GlaxoSmithKline). Gardasil is designed to prevent infection with HPV types 16, 18, 6, and 11 (HPV types 6 and 11 do not cause cervical cancer, but genital warts); Cervarix is designed to prevent infection from HPV types 16 and 18, which currently cause about 70% of cervical cancer cases. Both Gardasil and Cervarix are preventative (rather than therapeutic) vaccines, recommended for women who are 9 to 25 years old and have not contracted HPV. Pakistan is lucky in the aspect that it is a GAVI eligible country which qualifies for subsidized purchase of vaccines.

In conclusion, cancer cervix in the last decade in Karachi South has remained a malignancy with a low incidence. The cause of concern is the steady increase in the younger birth cohorts, the advanced disease at presentation; insignificant in-situ cancers and no preventive intervention or awareness practices in place.

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