RESEARCH COMMUNICATION

Rising Incidence of Gastric Malignancies in Karachi, 1995-2002

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Abstract

Introduction: South Asia is an enigma for gastric cancer, a low risk region with a contradictory high prevalence for *Helicobacter pylori*. Patients and Methods: To examine the demographics, pathology and trends of gastric cancer in Pakistan, epidemiological data of 335 gastric malignancies, registered at Karachi Cancer Registry (KCR) for Karachi South (KS), during 1st January 1995 to 31st December 2002 were reviewed. Trends were studied by categorizing the cases into two time periods '1995-7' and 1998-2002'. Results: Ninety six cases of gastric cancers were registered in the 1995-7 period, 61 in males and 35 in females. In males, the ASR (world), and crude incidence rate (CIR) per 100,000 were 3.9 and 2.3 respectively. In females, the values were 3.0 and 1.5. In the 1998-02 period 239 cases of gastric cancer were registered, 156 cases in males and 83 in females. The ASR and CIR per 100,000 were 6.0 and 3.4 in males and 3.6 and 2.1 in females. An 18% increase was observed in males and 14% in females during the seven year study period. The male to female ratio was 2:1.The mean age of male patients was 51.9 years [95% CI 45.8; 58.1; SD ±17.9] in 1995-7 and 53.7 years [(95% CI 51.6; 55.9; SD ±14.0] in 1998-02. In females the mean age for the two periods was 48.8 years (95% CI 42.5; 55.0; SD ±18.2] and 48.4 years [95% CI 45.4; 51.5; SD ±13.9] respectively. Age-specific curves showed a gradual increase in risk from the second until the seventh decade. The majority of the cases presented as poorly or moderately differentiated distal (non-cardia) cancers with a regional spread. Conclusion: Gastric cancers in Karachi fall into the prototype of a low risk developing country pattern. The incidence is increasing, most marked in males above 40 years of age. Larger pathology-based studies are required to comment on the precise morphological sub-types of gastric adenocarcinoma. Etiological studies focused on different strains of *H. pylori* are required to address the gastric cancer enigma, whilst examining possible protective environmental or genetic factors.

Key Words: Gastric cancer - Karachi, Pakistan - demographics - trends

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Introduction

Gastric cancer is the fourth most commonly diagnosed cancer worldwide and remains second only to lung cancer as the leading cause of cancer death (Parkin, 2004; Parkin et al., 2001). Despite reports of a decreasing incidence from developed countries, gastric cancer is a major health concern. The global incidence of gastric cancer remains fairly high with approximately 870,000 new cases and 650,000 deaths per year, two-thirds occurring in developing countries (Parkin, 2004).

The American Cancer Society (ACS) in 2009 listed Barrett's esophagus, *Helicobacter pylori* infection, male gender, age above 50 years, tobacco, diet (salted fish and meat, and pickled vegetables) and obesity as the major risk factors causing gastric cancers (Clark et al., 1994; Vaughan et al., 1995; Koizumi et al, 2004).

Pakistan, the study location is categorised as a low resource, developing country in South Central Asia. Karachi South (KS), the southern-most district of Pakistan is multiethnic with a fair representation of all socio-economic categories of the country. In the absence of a national cancer registration system, KS qualifies as a sample population of the country.

The present study was conducted with the objective of examining the incidence, pathology and trends of gastric cancer in Karachi.

Materials and Methods

Epidemiological data of incident gastric cancer 'International Classification of Diseases', 10th edition

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(ICD-10) category C16 registered at Karachi Cancer Registry (KCR) for Karachi South (KS), during 1st January 1995 to 31st December 2002 were reviewed (WHO, 1992). The morphological categories included were adenocarcinoma 8140/3, intestinal type 8144/3, diffuse type 8145/3, papillary adenocarcinoma 8260/3, tubular adenocarcinoma 8211/3, mucinous adenocarcinoma 8480/3, signet-ring cell carcinoma 8490/3, adeno-squamous carcinoma 8560/3, squamous cell carcinoma 8070/3, small cell carcinoma 8041/3, undifferentiated carcinoma 8020/3, carcinoid 8240/3, marginal zone B-cell lymphoma of MALT-type 9699/3, mantle cell lymphoma 9673/3, diffuse large B-cell lymphoma 9680/3 and GI stromal tumor 8936/3 (WHO, 2002; Hamilton SR, Aaltonen LA, 2000; Lauren P, 1965).

The present study included clinically diagnosed and microscopically verified cases. Variables recorded were the hospital patient-number, date of incidence, name, age, address, ethnicity, topography, morphology and grade. Manual and computerized validity check 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).

Crude, age-adjusted, and age-specific incidence rates were calculated using person years of population at risk by sex and 5-year age-groups, estimations based on the 1998 census assuming an annual growth rate of 1.94%. 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'. Incidence tables were based on ICD-10 (WHO, 1992). Trends were studied by categorizing the cases into 2 groups '1995-7' and 1998-2002'. The data were analyzed using SPSS 16.0.

Results

Three hundred and thirty five incident gastric cancers, registered at Karachi Cancer Registry (KCR) during 1st January 1995 to 31st December 2002 were reviewed. Ninety six cases of gastric cancers were registered in the 3 year period 1st January 1995 to 31st December 1997, 61 cases in males and 35 in females. In males the frequency of gastric cancer; ASR (world), and crude incidence rate (CIR) per 100,000 were 2.9%, 3.9 and 2.3 respectively. In females it was 1.7%, 3.0 and 1.5 respectively (Bhurgri et al., 2002).

During 1st January 1998 to 31st December 2002, 239 cases of gastric cancer were registered. One hundred and fifty six cases were registered in males, which accounted for 3.5% of all cancers, with an ASR and CIR per 100,000 of 6.0 and 3.4 respectively. In females the 83 cases registered accounted for 2% of all cancer cases. The ASR and CIR per 100,000 were 3.6 and 2.1 respectively (Bhurgri et al., 2007). Gastric cancer ranked 11th and 10th in males; 16th and 13th in females, in the 1995-7 and 1998-02 periods respectively. Between 1995 and 2002, an 18% increase was observed in males and 14% in females. The male female ratio for both periods remained 2:1.

Table 1. Demographics of Gastric Malignancies in Karachi South (1995-2002)

	Males		Females	
	95-97	98-02	95-97	98-02
ASR*	3.9	6.0	3.0	3.6
CIR*	2.3	3.4	1.5	2.1
Mean age	51.9	53.4	48.8	48.5
Religion				
Muslims	57 (93.4)	151 (96.8)	35 (100)	78 (94.0)
Christians	3 (4.9)	3 (1.9)	-	1 (1.2)
Hindu	1 (1.6)	2 (1.3)	-	4 (4.8)
Ethnicity				
Mohajirs	9 (14.8)	49 (31.4)	5 (14.3)	33 (39.8)
Punjabis	9 (14.8)	25 (16.0)	2 (5.7)	10 (12.0)
Sindhis	5 (8.2)	21 (13.5)	1 (2.8)	6 (7.2)
Baluchs	11 (18.0)	13 (8.3)	13 (37.1)	8 (9.6)
Memons	5 (8.2)	17 (10.9)	5 (14.3)	6 (7.2)
Pathans	6 (9.8)	17 (10.9)	2 (5.7)	6 (7.2)
Gujrati	2 (3.3)	12 (7.7)	2 (5.7)	6 (7.2)
Afghans	3 (4.9)	2 (1.3)	1 (2.8)	3 (3.6)
Unknown	11 (18.0)	-	5 (14.3)	5 (6.0)

*/100,000 population

The mean age of male gastric cancer patients was 51.9 years [95% CI 45.8; 58.1; SD ±17.9; range 58 years (22-80)] in 1995-7 and 53.4 years [(95% CI 51.2; 55.6; SD ±14.0; range 66 years (19-85)] in 1998-02. In females the mean age for the 2 periods was 48.8 years (95% CI 42.5; 55.0; SD ±18.2; range 64 years (16-80)] and 48.5 years [95% CI 45.5; 51.6; SD ±13.9, range 62 years (18-80)].

The age-specific curves showed a gradual increase in risk from the second until the seventh decade, followed by an apparent decrease in risk after the seventh decade in 1995-7 and a continuing rise in the 1998-02 period. The distribution by age, religion, ethnicity, education, occupation and marital status are given in table 1.

Table 2. Grade, Extent and Topography of Gastric Malignancies in Karachi (1995-2002)

	Males		Females	
	95-97	98-02	95-97	98-02
Grade (differentiation)				
Well	17 (27.9)	37 (23.7)	7 (20.0)	8 (5.1)
Moderately	15 (24.6)	52 (33.3)	11 (31.4)	30 (36.1)
Poorly	21 (34.4)	44 (28.2)	12 (34.3)	27 (33.2)
B-cell L	6 (9.8)	14 (9.0)	3 (8.6)	8 (9.6)
Unknown	2 (3.3)	9 (5.8)	2 (5.7)	9 (10.8)
Extent of spread				
Localized	18 (29.5)	42 (26.9)	7 (20.0)	13 (15.7)
Regional	27 (44.3)	78 (50.0)	17 (48.6)	46 (55.4)
Distant	9 (14.8)	12 (7.7)	7 (20.0)	7 (8.4)
Unknown	7 (11.5)	24 (15.4)	4 (11.4)	17 (20.5)
Topography- Stomach				
Cardia	2 (3.3)	18 (11.5)	2 (5.7)	10 (12.0)
Fundus	-	2 (1.3)	-	-
Body,	1 (1.6)	7 (4.5)	-	4 (4.8)
Antrum	12 (19.7)	47 (30.1)	15 (42.9)	15 (18.1)
Pylorus	-	5 (3.2)		4 (4.8)
Overlap	-	16 (10.3)	1 (2.9)	6 (7.2)
NOS	43 (70.5)	56 (35.9)	17 (48.6)	41 (49.4)

Table 3. Morphology of Gastric Malignancies in Karachi South (1995-2002)

	Males		Females	
	95-97	98-02	95-97	98-02
Morphology				
AC, NOS	29 (47.5)	55 (35.2)	17 (48.6)	19 (22.9)
Intestinal	8 (13.1)	26 (16.7)	4 (11.4)	7 (8.4)
Diffuse	5 (8.2)	20 (12.8)	5 (14.3)	13 (15.7)
Papillary AC	1 (1.6)	1 (0.6)	-	-
Mucinous AC	8 (13.1)	6 (3.8)	-	6 (7.2)
SRC	4 (6.6)	24 (15.4)	3 (8.6)	17 (20.5)

SRC, signet ring cell carcinoma

Microscopic verification was 95% (1995-7, males); 94% (1995-7, females), 96.3% (1998-02, males), 96.4% (1998-02, females).

Majority of the cases presented as poorly or moderately differentiated distal (non-cardia) lesions with a regional spread, in both genders. The predominant morphology was adenocarcinoma, diffuse, mucinous and signet ring cell types (Table 3).

Discussion

Globocan grades the world region into five categories, on a rising scale of 1 to 5 on the basis of the age standardized incidence rates of the country or the estimates of the same prepared by IARC. In males, the five categories in an ascending order are ASR world per 100,000 <5.2, <8.9, <14.1, <20.9 and <69.7. In females the five categories are ASR world per 100,000 <3.5, <5.2< 7.8, <11.1 and <30.6 (Parkin et al., 2001). Based on this scheme for gastric cancer, despite a rising incidence, Karachi South in the last decade remained in a low risk zone.

Globally, a twenty-fold variation is observed in the incidence of gastric cancer, (Parkin et al., 1993; Munoz N, 1988), with Japan and Korea having the highest rates in the world (Yamamoto, 2001; Ahn et al., 1991). Among men the ASR world, per 100,000 population for gastric cancers varied from the highest (80.3) in Japan to being the lowest (2.7) in Thailand (Curado et al., 2007). In women the incidence ranged from 1.0 per 100,000 in Trivandrum, India to 31.3 per 100,000 in Yamagata, Japan (Curado et al., 2007).

South and Central Asia are identified as low to moderate risk regions for cancer stomach. The incidence in males in the different cancer registries in India, on the south-east border of Pakistan, ranges from 3.4 per 100,000 in Delhi to 12.2 per 100,000 in Chennai and in females it ranges from 1 per 100,000 in Trivandarum to 6 per 100,000 in Chennai (Curado et al., 2007). Karachi with an ASR of 6.0 per 100,000 in males and 3.6 per 100,000 in females falls in the middle of this range. Iran, further north has a reported incidence of 11.2 per 100,000 persons and falls into a higher risk region, in comparison to Karachi (Marjani et al., 2007).

In Karachi, the male to female ratio for the entire 1995-2002 period remained 2:1, thus confirming an observation made for gastric non-cardia cancers globally (Nomura, 1996; Parkin et al, 2002; Crew and Neugut, 2006). The male to female ratio reported for gastric cardia carcinoma is higher, approximately 5:1 (Crew and Neugut , 2006).

The predominant site of involvement was the distal aspect of stomach and majority of the cancers were reported as adenocarcinoma, not otherwise specified. Where morphological categorisation was available, there was a predominance of diffuse type of adenocarcinoma with the signet ring and mucin secreting subtypes. Larger pathology-based studies are required to comment on the precise morphological patterns of gastric adenocarcinoma in Karachi.

Gastric adenocarcinoma arising in the proximal (cardia) and distal (non-cardia) stomach are reported as different biological entities with a geographical variation. Whereas the distal gastric cancers are declining in the more developed countries, the proximal tumors have been increasing in incidence especially amongst males (Crew and Neugut, 2006). The incidence of diffuse type gastric carcinoma, particularly the signet ring type, and the predominant pattern in Karachi has also been increasing but only in the developing countries (Henson et al., 2004).

Meanwhile, Parkin et al had reported higher incidence rates for distal gastric cancers in developing countries, whereas Munoz in 1988 had observed a predominance of the intestinal type of adenocarcinoma in high-risk areas and diffuse type in the low-risk areas (Munoz, 1988). Thus on the basis of the present observations, the incidence, topography and morphology of gastric cancers in Karachi fall into a typical prototype of low risk developing country pattern.

An established primary risk factor for gastric cancer is *H. pylori* infection and South Central Asia has been reported as a high prevalence area by Indian scientists, but the enigma remains that despite a rising incidence the region remains a low risk area (Singh and Ghoshal, 2006). It is an established fact that infection by *H. pylori* cagA+ strains is associated with an increased risk of severe atrophic gastritis and distal gastric cancer (Blaser et al., 1995; Parsonnet et al., 1997; Huang et al., 2003). A single lab-based study in Karachi on a small sample (50 cases) has reported a significant association of *H. pylori* with carcinoma stomach (Arif and Syed, 2007). Yet there are no reliable studies to substantiate these findings or provide an accurate assessment of *H. pylori* prevalence.

In conclusion, gastric cancers in Karachi fall into the prototype of a low risk developing country pattern. The incidence is increasing, most marked in males above 40 years of age. Larger pathology-based studies are required to comment on the precise morphological sub-types of gastric adenocarcinoma. Etiological studies focused on different strains of H. pylori are required to address the enigma of gastric cancer, whilst examining the possibilities of protective environmental or genetic factors.

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