RESEARCH COMMUNICATION

Increasing Incidence of Non-Hodgkin's Lymphoma in Karachi, 1995-2002

Yasmin Bhurgri[1,2,3], Shahid Pervez[2], Asif Bhurgri[1,3], Naveen Faridi[4], Ahmed Usman[5], Kazi LAG[6], Rashida Ahmed[2], Naila Kayani[2], Sheema H Hasan[2]

Abstract

This first population-based study of non- Hodgkin lymphoma (NHL) from any region in Pakistan, provides an overview of the incidence pattern and time trends in Karachi and generates hypotheses for future experimental research. Epidemiological data for 429 incident (1st Jan 1995 to 31st Dec 2002), microscopically verified nodal and extra-nodal NHL cases, registered at the Karachi Cancer Registry (KCR) for Karachi South, were reviewed. The age standardized incidence rate (ASIR) was 5.3/100,000 in males (M) and 4.1/100,000 in females (F), in 1995. A gradual increase in the annual incidence was observed during the study period, with NHL incidence rate increasing in 2002 to 8.4/100,000 in men and 6.5/100,000 in women, almost double the 1995 rates. NHL affected all age groups in both genders and for each group the ASIR was higher among men than women, with an overall gender ratio of 1.9. The mean ages of the patients were 41.5 years (95% CI 39.1; 43.8) in males and 44.0 years (95% CI 40.8; 47.1) in females. The adult to childhood ratios were 8.6 (M) and 10.7 (F). B-cell NHL comprised 81.0% of NHL in males and 87.3% in females. One fourth of the NHL cases were extra-nodal, the largest group was of gastrointestinal origin (54.1% M, 38.5% F). The gastric component was 21% M and 25.6% F.

Odds Ratios for sex, age-groups, ethnicity, religion, and subdivision by socio-economic categories were calculated by considering all malignancies, except lymphoproliferative disorders as controls. The odds ratio (OR) in men was 2.2 (95% CI 0.6; 3.0). Children and adolescents were at the highest risk of developing NHL, especially the 5-9 year olds, in both genders. A marginally higher risk was observed for the lower socioeconomic categories and for ethnicities belonging to Northern and North–Western Pakistan (Punjabi, Pushtu and Baluch) residing in Karachi South.

The incidence rates of NHL registered in Karachi South are likely to be a reflection of non-AIDS-associated NHL. Estimated HIV/AIDS incidence was too low during the study period in this population to have an impact on NHL incidence. The preponderance of low and intermediate grade lymphomas, paucity of central nervous system NHL and a higher childhood NHL component support this hypothesis. As yet unpublished reports, however, are raising the alarm on rising HIV positivity. NHL correlation with HIV/AIDS status and studies identifying risk factors of non- HIV/AIDS associated NHL (childhood viral infections, Hepatitis C virus, and Helicobacter pylori) are potential areas for future experimental and epidemiological research.

Key Words: non-Hodgkin's lymphoma - Karachi - pakistan

Introduction

This study was conducted with the objective of examining descriptive epidemiological characteristics, incidence and time trends of non-Hodgkin lymphoma (NHL) in Karachi (1995-2002). This is the first population-based study on NHL from any region in Pakistan and provides an overview of the incidence pattern of NHL in Karachi and generates hypotheses for future research.

Karachi, the largest city of Pakistan is located on the coast of Arabian Sea, latitude: 24 -56û-00" and longitude: 67 -01û-00", the Tropic of Cancer passes just below it. The Karachi Cancer Registry (KCR) provides population-based descriptive epidemiology data of cancer incidence by age, sex, race, and time period according to site and histological characterization for various populations. Karachi South is the oldest catchment population of KCR. This is the southern-most district of Karachi with a population of

[1]*Karachi Cancer Registry* [2]*Aga Khan University Hospital, Karachi* [3]*Sindh Medical College, Karachi* [4]*Liaquat National Hospital, Karachi* [5]*Jinnah Postgraduate Medical Centre, Karachi* [6]*Dow Medical College, Karachi Address all correspondence to:* [1]*Dr. Yasmin Bhurgri, Karachi Cancer Registry, Department of Pathology, Sindh Medical College, Rafiqui Shaheed Road, Cantt, Adjacent Jinnah Postraduate Medical Centre, Karachi, Pakistan. OR* [2]*Department of Pathology, Stadium Road P.O. Box 3500, Karachi 74800, Pakistan.*

1,724,915; 929,394 (54%) males and 795,521 (46%) females (Census 1998). It includes all ethnicities of the country, namely Sindhis, Punjabis, Pathans, Baluchs and Mohajirs with a fair representation of all socio-economic categories. In the absence of a national cancer registration system, it qualifies as a sample population of the country. A profound effect of westernization is seen in parts of this district, in stark contrast to an extreme cultural conservativeness in some parts and moderation in other parts of the same district. The cancer profile (ICD-10 categories) in Karachi South (WHO, 1992; Bhurgri, 2004) males is lung (C33-C34 - 11.7%; Age Standardized Incidence Rates- ASIR 25.5), oral cavity (C00-C06 - 13.1%; ASIR 22.5), larynx (C32 - 6.1%; ASIR 11.8), urinary bladder (C67 - 4.8%; ASIR 9.9), prostate (C61 - 4.1%; ASIR 9.8), lymphoma (C81-85;96 - 7.0%; ASIR 9.6), pharynx (C09-14 - 4.3%; ASIR 8.2), and colo-rectum (C18-21 - 4.4%; ASIR 7.8). In females the commonest cancers are breast (C50 - 34.6%; ASIR 69.1), oral cavity (C00-C06 - 8.9%; ASIR 8.9), cervix (C53 - 4.1% ASIR 8.6), esophagus (C15 - 3.7%, ASIR 8.6), ovary (C56 - 4.2%; ASIR 7.8), lymphoma (C81-85;96 - 3.5%; ASIR 7.2), gall bladder (C23-C24 - 2.6%; ASIR 5.8), and skin (C43-44 - 2.6%; ASIR 5.6).

Lymphoma (non Hodgkin Lymphoma and Hodgkin lymphoma) is a disease with global variation in its incidence. In males the ASIR ranges from 2.94 to 74.94 and in females from 1.86 to 63.9 (Parkin, 2002). The World Health Organization (WHO) modification of the Revised European-American Lymphoma (REAL) Classification categorizes malignancies of lymphoid cell origin (lymphoma and leukemia) into major groups on the basis of morphology and cell lineage. The categories include B-cell neoplasm, T-cell/natural killer (NK)-cell neoplasm, and Hodgkin lymphoma. The following discussion pertains to B and T cell NHL (Harris et al 1994; Harris et al 1999).

NHL, International Classification of Diseases 10th Revision (ICD-10) categories C82-85;96 is a heterogeneous group of lymphoproliferative malignancies with differing patterns of behavior and responses to treatment (Armitage, 1993). The malignancy usually originates in the lymphoid tissues and can spread to other organs. The prognosis depends on the histologic type, stage, and treatment.

Methodology

Epidemiological data of incident NHL cases, ICD-10 (International Classification of Diseases 10th Revision) categories (C82-85;96), registered at KCR for Karachi South, during 1st January 1995 to 30th June 2004 were reviewed. The study included microscopically verified NHL, nodal and extra-nodal sites and excluded Hodgkinûs lymphoma (ICD-10 category C81).

To ensure maximally complete data, cases registered during 1st January 1995 to 31st December 2002 were considered for the present study. The most recent cancer data, although adequate for cancer surveillance, becomes more complete with late reports of additional cancer cases thus slightly increasing the incidence rates. Therefore for registration purpose a window period of 1-2 years is essential for data completion.

The reported cancer data were rechecked, and residency status re-ascertained. People residing in the specified geographical regions for more than six months were considered residents. The cases were categorized by tumor site, age and sex of the patient. Variables recorded were the hospital patient-number, date of incidence, name, age, sex, address, ethnicity, topography, morphology, B and T cell type, grading and staging. The data were classified using ICD-O3 (International Classification of Diseases-Oncology, 3rd edition) and computerized using a customized version of CANREG-3 software (Fritz et al 2000).

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). This involved factors influencing comparability i.e. classification and coding (Parkin et al, 1994). Tumors were categorized according to the WHO modification of the REAL system, to standardize with other parts of the world (Harris et al 1994; Harris et al 1999). Lymphomas were grouped by site into nodal (ICD-O-3 site codes C770-779) and extra-nodal lymphoma; the later included all NHL sites except ICD-O3 site codes C770-779 (Fritz et al 2000).

Crude, age-adjusted, and age-specific incidence rates of NHL were calculated for each sex. 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 ASIR for each year. The data are presented by calendar year to examine the secular trends. Incidence trends were plotted using a linear regression analysis. Logarithmic transformation (equation $y = 0.3817x + 3.5583$ and an R^2 value of 0.8502) was preferred specifically because this facilitates the comparison of trends at varying incidence levels. To determine the socio-economic profile, the district was divided into 3 subcategories based on the income of approximately 70% of the resident population. The categories ranged from 1 to 3 in an ascending income strata (Table 1). Category I was composed of the predominantly financially deprived class with an annual income of less than $2000, and a low literacy level. Residents of category II had an annual income range of $2001-$20,000 with a moderately high literacy. Category III was largely made up of educated professionals, with an annual income of more than $20,000. A sample survey was

conducted to categorize the financial status of the population. All specimens for 1998-2002 were initially evaluated on Hematoxylin and Eosin (H&E) stained sections and subsequently immunohistochemical analysis was performed by employing envision technique. The antibodies used in immunohistochemical staining included Leukocyte Common Antigen (LCA), Pan B (CD20, CD79), Pan T (UCHL), Bcl 2, Mib 1(Ki 67) and Cyclin D1. Prior to 1998, immunochemical typing was not a routine practice.

Odds Ratio for sex, age-groups, ethnicity, religion, and subdivision by socio-economic categories were calculated by considering all malignancies (except lymphoproliferative disorders) for each group, registered at KCR for the same period (1st January 1995 to 31st December 2002) as controls. The malignancies considered were ICD-O3, morphological categories, M-8000 to M-8991 (Fritz et al 2000). The data were analyzed using SPSS 11.0.

Results

A total of 429 lymphomas were registered at the Karachi Cancer Registry for Karachi South during an eight year period, 1995-2002. The age standardized incidence rate (ASIR) was 5.6/100,000 in males and 4.3/100,000 in females. A slow upward variation in the annual incidence was observed during the study period. In 1995 the NHL incidence rate in men was 5.3/100,000; by 2002 it had increased, almost doubled to 8.4/100,000. Among women, the 1995 NHL incidence rate was 4.1/100,000, rising to 6.5/100,000 by 2002 (Figure 1). The increase in the incidence affected all age groups in both genders (Figures 2 and 3).

The mean age of the male patients was 41.5 years (95% CI 39.1; 43.8) and of females 44.0 years (95% CI 40.8; 47.1). The age ranges were 93 years in males (minimum age 2 years; maximum 95 years) and 82 years in females (minimum age 3 years; maximum 85 years). The mean age of childhood lymphoma was 7.9 years (95% CI 6.3; 9.4) in
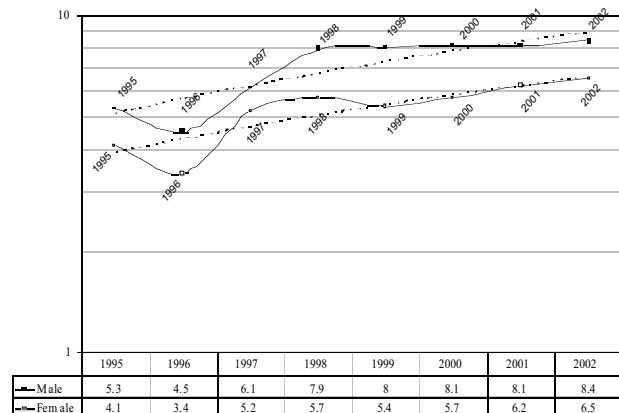
males and 8.4 years (95% CI 6.1; 10.6) in females. The youngest male patient was 2 years and the youngest female patient was 3 years; the oldest male and female children were 14 and 13 years respectively. The mean age of adult NHL was 45.3 years (95% CI 43.2; 47.5) in males and 47.6 years (95% CI 40.4; 44.7) in females. The gender ratio (M:F) was 1.9, the odds ratio (OR) in men was 2.2 (95% CI 0.6; 3.0) and in females 0.4 (95% CI 0.3; 1.3). The component of childhood NHL was 10.4% and 9.3% in males and females respectively. The adult to childhood ratio (A:C) was 8.6 in males and 10.7 in females. B-cell NHL comprised 81.0% of NHL in males and 87.3% in females, the rest were of T-cell or NK cell origin.

Children and adolescents were at the highest risk of developing NHL; 0-4 years OR 4.5 (95% CI 0.3; 6.7) in males, 5.4 (95% CI 0.3; 9.8) in females; 5-9 years, OR 8.9 (95%CI 0.2; 12.2) in males, 10.1 (95% CI 0.2; 16.4) in females; 10-14 years, OR 5.0 (95% CI 0.3; 6.7) in males, 5.8 (95% CI 0.3; 8.2) in females and 15-19 years OR 4.7 (95% CI 0.3; 6.7) in males, 5.0 (95% CI 0.3; 7.4) in females.
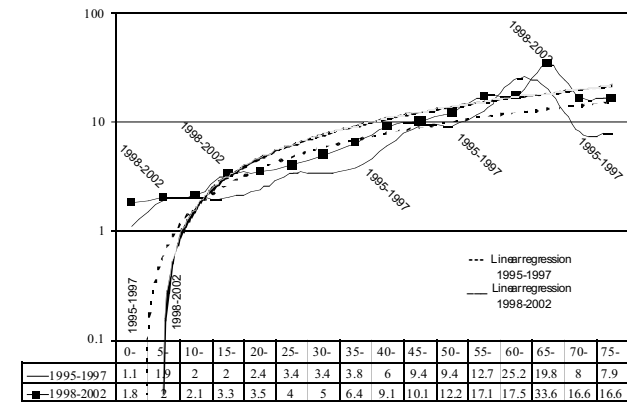
	0-	5-	10-	15-	20-	25-	30-	35-	40-	45-	50-	55-	60-	65-	70-	75-
1995-1997	1.1	1.9	2	2	2.4	3.4	3.4	3.8	6	9.4	9.4	12.7	25.2	19.8	8	7.9
1998-2002	1.8	2	2.1	3.3	3.5	4	5	6.4	9.1	10.1	12.2	17.1	17.5	33.6	16.6	16.6

Figure 2. Age Specific Incidence Rates (Non-Hodgkins Lymphoma) Males Karachi South 1995-2002. The Trends (logistic regression) show an increased incidence in all age groups.

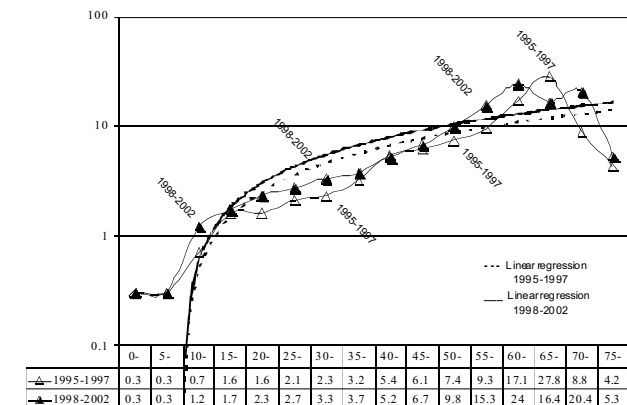|	0-	5-	10-	15-	20-	25-	30-	35-	40-	45-	50-	55-	60-	65-	70-	75-
1995-1997	0.3	0.3	0.7	1.6	1.6	2.1	2.3	3.2	5.4	6.1	7.4	9.3	17.1	27.8	8.8	4.2
1998-2002	0.3	0.3	1.2	1.7	2.3	2.7	3.3	3.7	5.2	6.7	9.8	15.3	24	16.4	20.4	5.3

Figure 3. Age Specific Incidence Rates (Non-Hodgkins Lymphoma) Females, Karachi South, 1995-2002. The Trends (logistic regression) show an increased trends in all age groups.

	1995	1996	1997	1998	1999	2000	2001	2002
Male	5.3	4.5	6.1	7.9	8	8.1	8.1	8.4
Female	4.1	3.4	5.2	5.7	5.4	5.7	6.2	6.5

Figure 1. Gender Specific Time Trends for (Non-Hodgkins Lymphoma) in Karachi South 1995-2000. An apparent decrease in 1996 in both genders, is depictive of undercoverage followed by a compensatory increased coverage in 1997, and subsequent stabilisation of rates. These fluctuations may be seen in early years of registration.

There was a subsequent gradual fall in the OR for all age groups (Table 1).

One fourth of the NHL cases were of extra-nodal origin. The largest group of extra-nodal NHL was gastrointestinal (66.7% males; 48.7% females). Twenty one percent of the extra nodal NHL in males and 25.6% in females were of gastric origin, 15.3% in males and 7.7% in females were of small intestine origin and 5.6% in males and 5.1% in females were of colorectal origin. All were B-cell type. The other important extra-nodal sites were bone (M 8.3%; F 7.7%), skin (M 6.9%; F 7.7%), and CNS (M 5.5%; F 5.1%). Amongst males the other common sites were testes (4.2%),

prostate (1.4%), lung (2.8%), and larynx (1.4%). Amongst females exclusive sites were breast (5.1%), ovary (15.4%) and thyroid (10.3%).

Morphological subcategorization was possible for 1998-2002 cases only. Eighty percent were mature B cell lymphomas, 20% were T cell and NK cell lymphomas. Two thirds of the B-cell lymphomas were the diffuse large B-cell category (65.0%). The remaining were small B-cell (10.0%) and Burkitts lymphomas (10.0%). Other categories formed a very minor component. There were no cases of secondary NHL.

The odds ratio for socioeconomic residential gender stratified categories remained between 0.76 and 1.3 with a slightly higher risk in the lower socio-economic categories. A marginally higher risk was also observed for ethnicities belonging to the Northern, NorthñWestern Pakistan, i.e. the Punjabi, Pushtu and Baluch ethnicites (Table 1).

Discussion

Gender specific time trends for NHL in Karachi South 1995-2002; showed a steadily increasing incidence during the eight year period from 1995 to 2002. Muller et al in 2004 have reported an increasing incidence of all etiological subgroups of NHL, AIDS-associated and non-AIDS-associated, globally. NHL a disease with global variations is the tenth most common cancer in males in Karachi South and the ninth in females. An institutional-based study from Lahore has cited NHL as the second most important malignancy in males; however the study could be depictive of a selection bias, as it is a single referral institution data (Aziz et al, 2003). Yet, one cannot entirely ignore this observation as a bias. A higher risk for NHL has been observed in the Karachi South data for individuals of ethnicities from northern areas of Pakistan and the Lahore data represents one such ethnicity, the Punjabi ethnicity. Further research needs to be conducted in different geographical regions of Pakistan, as the ethnic origin is varied in different areas. The Aga Khan University pathology-based cancer registry has also reported a lymphoma bias (Bhurgri et al 2002).

In Karachi the age specific incidence rates in both genders show a rising incidence in all age groups, particularly in the young and the elderly (figures 2 and 3). This rise has been noted worldwide, particularly in elderly persons above 55 years (Muller et al 2004). In United States (US) NHL is the fifth most common cancer (Baris and Zahm, 2000). The ASIR was 16.8 in males in 1993-97 and 10.6 in females (Parkin et al 2002). NHL incidence rates have increased more than 50% over the past 15 years, making it the sixth leading cause of death from cancer in the US and the fourth most significant malignancy in terms of economic impact (Muller et al 2004). Despite a rising incidence, the NHL incidence in Karachi remains below 10/100,000. United States has registered a dramatic rise in the incidence with comparable trends worldwide (Liu S et al 2003; Zheng et al 1992). These dramatic changes in the NHL incidence are a reflection of

Table 1. Frequency and Odds Ratio of Cases on the Basis of Age-groups, Residence, Religion and Ethnicity

Age groups	Frequencies		Odds Ratio (95% Confidence Intervals)	
	Male %	Female %	Male	Female
0-4	3.3	2.3	4.5 (0.3; 6.7)	5.4 (0.3; 9.8)
5-9	7.7	6.2	8.9 (0.2;12.2)	10.1 (0.2;16.4)
10-14	5.9	6.1	5.0 (0.3; 6.7)	5.8 (0.3; 8.2)
15-19	6.9	7.0	4.7 (0.3; 6.7)	5.0 (0.3; 7.4)
20-24	5.1	4.5	2.6 (0.6; 3.3)	1.9 (0.8; 2.7)
25-29	5.2	5.6	2.3 (0.6; 3.0)	1.5 (0.5; 2.0)
30-34	5.2	4.8	1.4 (0.9; 1.8)	0.9 (0.4; 1.7)
35-39	6.1	7.8	1.4 (0.9; 1.7)	0.9 (0.2; 1.5)
40-44	7.8	7.3	0.9 (0.1; 1.4)	0.6 (0.2; 2.2)
45-49	7.1	7.7	0.8 (0.1; 1.5)	0.6 (0.2; 2.2)
50-54	9.3	7.7	0.8 (0.1; 1.5)	0.6 (0.2; 2.2)
55-59	7.1	7.7	0.7 (0.1; 1.8)	0.9 (0.8; 1.5)
60-64	9.1	11.1	0.6 (0.1; 2.0)	0.9 (0.1; 1.4)
65-69	5.8	6.2	0.5 (0.2; 2.7)	0.8 (0.1; 1.7)
70-74	4.9	5.2	0.5 (0.2; 2.7)	0.9 (1.2; 1.5)
75-79	1.9	1.5	0.4 (0.1; 3.7)	0.5 (0.2; 3.7)
80-84	1.0	0.9	0.4 (0.1; 4.5)	0.6 (0.4; 3.7)
85+	0.5	0.4	0.5 (0.1; 4.5)	0.6 (0.4; 5.5)
Subdivisions	Male %	Female %	Male	Female
Category I				
City	32.9	32.5	1.2 (0.9; 1.6)	1.3 (0.9; 1.8)
Category II				
Garden	12.5	17.9	1.1 (0.7; 1.5)	1.0 (0.7; 1.6)
Eidgah	8.9	7.3	0.9 (0.6; 1.6)	0.9 (0.5; 1.7)
Arambagh	8.2	6.6	0.8 (0.4; 1.4)	0.9 (0.5; 1.7)
Preedy	6.4	7.3	1.2 (0.7; 2.2)	1.2 (0.7; 2.3)
Category III				
Saddar	23.6	19.2	0.8 (0.2; 1.2)	0.8 (0.5; 1.2)
Civil Lines	7.5	9.3	1.0 (0.6; 1.6)	0.9 (0.5; 1.6)
Religion	Male	Female	Male	Female
Muslim	96.4	94.0	1.1 (0.9; 3.9)	0.8 (0.4; 1.6)
Christian	1.4	2.7	0.8 (0.3; 2.6)	1.2 (0.4; 3.3)
Hindus	1.8	2.0	0.9 (0.3; 2.7)	1.2 (0.4; 3.7)
Parsees	0.4	0.7	1.4 (0.2; 9.9)	1.9 (0.3; 14.9)
Ethnicity	Male	Female	Male	Female
Sindhi	15.0	15.2	1.0 (0.2; 1.6)	1.2 (0.9;1.9)
Punjabi	22.1	19.7	1.6 (0.9; 2.4)	1.2 (0.8;1.4)
Pathan	15.8	6.1	1.7 (1.0; 2.7)	0.8 (0.8;1.2)
Baluch	22.1	19.7	1.9 (1.2; 2.9)	1.7 (0.1;1.2)
Mohajir	25.0	39.3	0.6 (0.4; 0.9)	0.7 (0.3;0.9)

the AIDS epidemic. The incidence of NHL is greatly increased in human immunodeficiency virus (HIV) infected individuals, an association first observed in the eighties (Hiddemann, 1989; Hartge et al 1994; Knowles, 1997). NHL reflects the AIDS status in the population. In San Francisco, NHL rates among white men rose from 10.7 in 1973 to an epidemic peak of 31.4 in 1995 and then declined to 21.6 in 1998, reflecting a decline in the number of individuals with AIDS and improved immune function in such individuals following the introduction of effective antiretroviral therapies in the 1990s. Nonetheless the incidence of NHL types not considered AIDS-associated and of NHL in groups at low risk of AIDS, such as men aged 55 years and older and women of all ages, has also continued to increase throughout the 1980s and 1990s (Eltom et al, 2002).

In Karachi the increase in the incidence is more likely to be the non-AIDS-associated variety, the HIV prevalence being low in the study period in this population. Pakistan is identified as a low risk population for HIV infection. The prevalence of AIDS in the study population has been very low till now, limited to sporadic cases in Pakistanis (and their sexual partners) who have traveled abroad, or overseas contract workers (Baqi et al 1999). The national estimates of HIV prevalence was 64 per 100,000 (0.064%) in 1998, but with first warnings of an emerging epidemic (Hyder and Khan, 1998). As no year-wise national estimates for HIV/ AIDS are available for Pakistan, it would be premature to correlate the rise in NHL incidence in Karachi South with HIV/AIDS. If there is an association, it is very subtle, being superimposed on a much higher background incidence of NHL in individuals without HIV/AIDS.

The risk factors of non-AIDS-associated NHL are a causal link between infectious agents, and lymphomagenesis, particularly human T-cell leukemia/lymphoma virus type 1 (HTLV-1) in adult T-cell lymphoma/leukemia; human herpesvirus 8 (HHV 8) in body cavityñbased lymphomas in patients with HIV infection, and Epstein-Barr virus (Burkitt lymphoma, sinonasal lymphoma in Asia and South America, lymphomas in immunocompromised patients), Hepatitis C-virus and Helicobacter pylori (gastric MALT lymphoma) infections (Thorburn et al 1996; Joab et al, 1999; Timuraglu et al 1999). There are few studies from this population giving evidence of the prevalence of Epstein-Barr virus, a viral cofactor implicated primarily in the development of primary brain lymphomas (Noorali et al 2003; Cingolani et al 2000, MacMahon et al 1991) and also in some peripheral-site NHLs in individuals with AIDS (Cohen et al 1991).

The development of NHL is also influenced by endemic geographical factors, e.g. in Africa, the incidence of Burkitt lymphoma is 5.7-7.6 per 100,000 population as compared to 0.1 per 100,000 population in the US. The significance of exposure to environmental agents and occupational risk is uncertain. Increased risk with solar ultraviolet exposure, an increased risk in farmers; pesticide and herbicides applicators; flour millers; meat workers; painters; mechanics; and workers in the petroleum, rubber, plastics, and synthetics industries have been observed (McMichael and Giles 1996;

Baris and Zahm, 2000; Ferris et al 2001; Eltom et al 2002; Muller et al 2004). Chemicals that have been linked to development of NHL include solvents and organic chemicals (e.g. benzene, carbon tetrachloride), and wood preservatives.

Morphologically, approximately half the 1995-1997 NHLs were not further subcategorized as immunochemistry was not cost effective for a majority of the patients or laboratories at the time. Also, in the earlier years of registration the techniques were not fully established or freely available in Karachi, neither were accurate classification systems. After 1998 immunochemistry with subcategorisation of NHL with REAL and subsequently the WHO modification was implemented. In this data, large B-cell, diffuse NHL was the most common category reported followed by the small B-cell lymphocytic lymphoma.

The preponderance of low and intermediate-grade NHL, a higher risk in children and the paucity of central nervous system (CNS) lymphomas, support the hypotheses of non-AIDS associated NHL in the population. A few types of NHL have been associated with AIDS, notably CNS lymphomas, high-grade immunoblastic and Burkitt's lymphomas and to a lesser extent, intermediate grade large cell diffuse lymphomas. In contrast, most low and intermediate-grade lymphomas are not AIDS-associated, including small-cell lymphocytic and follicular lymphomas (Biggar, 2001). This pattern is somewhat different from other Asian populations which have higher rates of aggressive NHL, T-cell lymphomas, and extranodal disease. In the Middle East, high rates of intestinal extranodal disease are observed (Muller et al 2004). The incidence of specific NHL histologic types is reported to be changing with some types rising and others falling (Groves et al, 2000).

The ASIR for NHL are higher among men than women in Karachi, this is a global observation in every racial/ethnic group (Muller et al 2004). The childhood NHL component is higher then the rates reported by the American Cancer Society (ACS) estimates (95% NHL occur in adults, 5% in children). The average age for NHL in Karachi South is 2 decades younger then ACS estimates for the US (average age at diagnosis is 60 years). This supports an infective basis of lymphomagenesis in the study population and identifies an area for experimental research.

There were no cases of secondary NHL. The probable reason is the lack of proper treatment, and overall poor survival of cancer patients, secondary NHL is a result of cancer therapy. We are not missing cases of secondary NHL as developing a secondary NHL more than 12 months after treatment for first cancer, is uncommon and our cases are followed for life (Cappelaere, 1998).

Like other registry-based studies, our study has potential limitations. The incidence of NHL that we report may not be directly applicable to the entire population of Pakistan as risk factors and incidence of AIDS vary by community and AIDS status is different for different regions in of Pakistan. Other limitations of this study include the lack of individual data on HIV status of cases.

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