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The burden of non-Hodgkin lymphoma in Central and South America☆

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ABSTRACT

Rationale and objective: The burden of non-Hodgkin lymphoma (NHL) has increased in some Central and South American countries. We describe the current patterns and trends in NHL incidence and mortality in Central and South America.

Methods: We obtained regional- and national-level incidence data from 48 population-based cancer registries in 13 countries, and national-level cancer mortality data from the WHO mortality database for 18 countries. We estimated world population age-standardized incidence rates (ASRs) and mortality rates (ASMRs) per 100,000 person-years for 2003–2007, and presented distributions by histological subtype.

Results: NHL incidence and mortality rates varied between countries by 2–8- and 6-fold, respectively. ASRs per 100,000 ranged from 1.4 to 10.9 among males and 1.3–9.2 among females. Corresponding ASMRs were between 0.5 and 4.8 among males and between 0.5 and 3.0 among females. The highest incidence was observed in Uruguay (males), Ecuador, Peru and Colombia (males). The highest mortality was seen in Uruguay and Costa Rica. Trends in NHL incidence and mortality in Argentina, Brazil, Chile and Costa Rica did not show marked changes. B-cell neoplasms and NHL not otherwise specified (NOS) accounted for 44% and 34% of all NHL cases. Diffuse large B-cell lymphoma, NOS, was the most frequent histological subtype.

Conclusion: The geographic variations in NHL rates may partially reflect differences in registration practices, disease classification, diagnostic practice, and death certification quality. There is a need for high-quality data and improvements in the accuracy of NHL histological diagnosis. Given the expected increase in NHL, careful monitoring of rates remains a priority to guide cancer control programs.

1. Introduction

Non-Hodgkin lymphoma (NHL) represents a heterogeneous group of lymphoproliferative malignancies with different morphology, immunological phenotype, genetics, molecular biology and clinical features [1,2]. NHL is the tenth most frequent cancer diagnosis and the 11th leading cause of cancer death in the world, with estimates of nearly 400,000 new cases and 200,000 deaths having occurred in 2012 [3]. NHL incidence and mortality rates vary considerably across the globe, and rates are higher in males than females [4–7]. The highest NHL incidence rates are seen in North America, Europe, Oceania, and some African countries [6], whereas the highest mortality rates are observed in New Zealand, Israel and Canada [8]. These geographical variations may be related to differences in demographic, environmental and other factors [6].

Rapid increases in NHL incidence and mortality rates have been reported in the United States and some European countries over the last few decades, but more recently rates have stabilized or declined [1,6,9–11]. Although the reasons for the observed patterns are not completely understood, improvements in disease diagnosis and changes in disease classification may partially explain the increases in incidence, while improvements in treatment for some NHL types may explain, at least in part, the declines in mortality. Changes in exposure to risk factors, including some infectious agents and immunosuppressive drugs, may also be responsible for some of the observed patterns [1,4,6,7,12,13].

Central and South America carry approximately 7% of the global burden of NHL, with an estimated 27,000 new cases and

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14,000 cancer deaths, making NHL the ninth most common diagnosis and the 11th most common cause of cancer death in 2012 [3]. Increases in NHL incidence have been reported in Brazil and Colombia from the 1970s and 1980s [14], and increases in mortality have been reported in Colombia and Mexico since the late 1990s [15,16]. Recent GLOBOCAN estimates have indicated that, by the year 2030, the burden of this disease will increase in the region by more than 60% (to 43,000 new cases and 24,000 deaths), mainly because of aging and growth of the population [3]. Given the scant information available on the burden in Central and South America, we describe in this paper the incidence and mortality patterns and trends in NHL in Central and South America (including previously unpublished incidence data), and discuss our results in light of factors associated with an increased risk of NHL.

2. Methods

The present analysis includes all cases registered as non-Hodgkin lymphoma (C82–C85 and C96), as coded by the 10th edition of the International Classification of Diseases for Oncology (ICD-10). The data sources and methods are described in detail in an earlier article in this issue. In brief, we obtained regional- and national-level incidence data from 48 population-based cancer registries in 13 countries, and national-level cancer death information from the World Health Organization (WHO) mortality database for 18 countries. We estimated age-standardized incidence (ASR) and mortality (ASMR) rates per 100,000 person-years using the direct method and the World standard population [17,18]. We estimated national ASRs by aggregating the data from the available cancer registries using a weighted average of local rates. Registries that provided formal consent to use data by individual year of diagnosis for $\geq$10 years were included in the time-trend analysis (Table 1). To describe incidence and mortality time trends, we calculated the estimated annual percentage change (EAPC) for the most recent 10-year period using the method proposed by Esteve et al. [19]. All of the EAPCs were tested for equality to zero by using the corresponding standard errors. We considered EAPCs statistically significant if the P-value ≤ 0.05. We conducted the data analysis in Stata version 12.1 (StataCorp) [20].

We also present the distribution of NHL by histopathological categories. NHL tumors were classified according to the revised WHO classification system [21] and used in Cancer Incidence in Five Continents [22]. To avoid potential misclassification of NHL subtypes, all codes were checked with the IARCcrgTools conversion program provided by IARC (ICD-O-3 to ICD-10) [23]. For comparative purposes, refined histological classifications are also presented [24].

3. Results

In the most recent 5-year period about 19,000 cases and 52,000 deaths from NHL occurred in Central and South America, accounting for 3% of the total cancer burden in both sexes; it is among the 14 most frequently diagnosed cancers, and between the 6th and 14th most common cause of cancer-related death (Table 1). Approximately 64% (range 55–79%) of the NHL cases were diagnosed in men and women aged $\geq$50 years; 33% (range 20–39%) of the cases were diagnosed under the age of 50 years, and in 3% (range 0–9%) of the cases the age at diagnosis was unknown (Fig. A1).

3.1. Age-standardized incidence and mortality rates

Overall, males had higher incidence and mortality rates than females (male-to-female ratios ranging from 1.1 to 2.6:1 and from 1.1 to 1.6:1, respectively, except in El Salvador). ASRs of NHL ranged from 1.4 to 10.9 per 100,000 among males and from 1.3 to 9.2 per 100,000 among females. The highest ASRs in both sexes were observed in Uruguay (males), Ecuador, Peru and Colombia (males), while the lowest were in Bolivia and El Salvador. ASMRs ranged between 0.5 and 4.8 per 100,000 among males and between 0.5 and 3.0 per 100,000 among females. The highest mortality rates for both males and females were seen in Uruguay and Costa Rica, whereas the lowest were in Guatemala and El Salvador (Table 2).

3.2. Time trends

Incidence and mortality rates of NHL in the four countries evaluated did not showed marked changes over time (Fig. 1). In the most recent 10-year period, the largest increases in NHL incidence rates were seen in Costa Rica (EAPC: 1.5% for males and 2.7 for females, $P > 0.05$) whereas the largest decline occurred in Chilean males (EAPC: -2.9, $P > 0.05$). The largest increase in mortality was seen in Costa Rica (EAPC: 2.8 for males and 5.9 for females, $P > 0.05$) while the largest decline was in Argentinean females (EAPC: -1.3, $P > 0.05$) (Fig. 2).

3.3. Distribution of NHL incident cases by histological subtype

In the most recent 5-year period, 44% (range 2–78%) of all the NHL cases diagnosed in Central and South America were B-cell neoplasms, 34% (range 8–62%) were NHL not otherwise specified (NOS), 14% (range 4–22%) were unspecified malignant neoplasms, and 7% (range 0–16%) were T-cell and NK-cell neoplasms (Table 3).

The (median) age at diagnosis was 59 years (range 0–100) for B-cell neoplasms, 55 years (range 0–100) for T-cell and NK-cell neoplasms, 60 (range 0–100) for NHL, NOS, 14 years (range 0–92) for other specified, and 58 years (range 0–100) for unspecified malignant neoplasms (Table 3).

Diffuse large B-cell lymphoma (DLBCL) NOS was the most frequently diagnosed B-cell neoplasm, accounting for 40–62% of all the cases diagnosed in this category, except in Cuba where small-cell B-cell and Burkitt lymphoma were more common (43% of the cases). Follicular lymphoma was also a frequent diagnosis in the region, accounting for 8–21% of the B-cell neoplasm cases (except for Chile with 3%), followed by small-cell B-cell lymphoma (range 7–22%) and marginal-zone B-cell lymphoma, NOS (range 3–15%, except for Cuba and El Salvador with 0%) (Table 4).

Among the T-cell and NK-cell neoplasms (Table 5), mature T-cell lymphoma NOS was the most frequently diagnosis, accounting for 15–50% of all the tumors within this category (except for Bolivia and Cuba, with no recorded cases) followed by and cutaneous T-cell lymphoma NOS (14–42%, except for Bolivia, Cuba, and French Guyana, with 0 cases).

Table 1
Countries included in the analysis of time trends.

Country	Names of registries included	Period	% of the population covered
Argentina	Bahia Blanca	1993–2007	0.8
Brazil	Aracaju, Fortaleza, Goiania, Sao Paulo	1997–2006	8.0
Chile	Valdivia	1993–2008	2.2
Costa Rica	National registry	1985–2007	100.0