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Hodgkin lymphoma burden in Central and South America☆

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ABSTRACT

Rationale and objective: Hodgkin lymphoma (HL) is largely curable owing to improvements in treatment since the 1960s; nevertheless, high mortality rates have been reported in Central and South America. We describe the current burden of HL in the Central and South American region.

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

Results: HL incidence rates varied 7-fold in males and 11-fold in females (male-to-female ratio 1:1–2.5:1). The highest ASRs were seen Argentina, Brazil, Costa Rica (males), Cuba (males) and Uruguay (females), whereas the lowest were in Bolivia and El Salvador. ASMRs varied by 4-fold in males and 6-fold in females (male-to-female ratio 1:1–4.3:1), with ASMRs <0.7 for most countries, except Cuba (≥ 1.0). In most countries, age-specific incidence rates of HL showed a bimodal pattern. Trends in HL in Argentina, Brazil, Chile, and Costa Rica remained stable in 1997–2008. Of all HL cases, 48% were unspecified as to histological subtype. Nodular sclerosis and mixed cellularity were the most frequent histologies.

Conclusion: The geographic variation in HL across the region may in part reflect differences in data quality and coverage, and differences in the adoption of modern therapies and healthcare access. Our results highlight the need for high-quality data and increased coverage in order to provide vital guidance for future cancer control activities.

1. Introduction

Despite Hodgkin lymphoma (HL) accounting for no more than 0.5% of the total cancer burden worldwide in 2012 [1], its unusual biology and epidemiology and positive response to treatment has drawn the attention of clinicians, pathologists and researchers [2]. HL is classified – on the basis of differences in histology, morphology and immunophenotype of the tumor cells – into two major types: classical HL (cHL) and nodular lymphocyte-predominant HL (NLPHL), accounting for 95% and 5% of all HL cases, respectively [3]. cHL is further subdivided into nodular sclerosis (NS), mixed cellularity (MC), lymphocyte-rich, and lymphocyte-depleted types [4]. Initial treatment is based on histological characteristics, stage at diagnosis, and other prognostic factors [5]. HL is largely curable owing to improvements in treatment since the 1960s [6,7], with survival rates of 80.8% and 85.2% in Europe and in the United States, respectively [7,8]. Although the etiology of HL is complex and poorly understood, comparisons in age-specific incidence rates of HL, specific incidence patterns by sex and socioeconomic status for specific subtypes of HL have provided critical clues in the etiology of this disease [2,9–13]. For instance, age-specific incidence rates of HL are bimodal, with the first peak occurring at age 15–34 years and the second after age 60 years, specifically in European, American, Hispanic and Australian populations [14], whereas in developing countries the incidence of HL is characteristically high in early childhood and among the oldest age groups. Affluent standards of living during early

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childhood have been associated with an increased risk of young-adult HL, suggesting a delayed exposure to a common infectious agent, while the opposite is true for children living in less favorable living conditions [12,13,15].

GLOBOCAN estimates indicated that nearly 66,000 HL incident cases and more than 25,000 HL deaths occurred globally in 2012, with the vast majority (56% and 75%, respectively) occurring in less developed regions of the world. (Developed regions include all regions of Europe, Northern America, Australia/New Zealand and Japan. Less developed regions include: all regions of Africa, Asia (excluding Japan), Latin America and the Caribbean, Melanesia, Micronesia and Polynesia.) Approximately 8–9% of the global burden of new HL cases and deaths were estimated to occur in the Central and South American region [1,16]. Recent predictions indicate an increase of 54% in the absolute number of HL cases in Central and South America for the year 2030, owing to growth and aging of the population [1,16].

Declines in HL mortality have been reported in Europe, the United States and Japan over the last few decades, largely because of the adoption of modern therapies [17,18]. Declines in HL mortality have also been described in several Latin American countries (including the Caribbean) in the past decade. In spite of the reported declines, elevated mortality rates occurred in Costa Rica, Cuba, Mexico and Venezuela, probably reflecting differences in healthcare access and management of this disease [6,19,20]. Unfortunately, HL incidence data in the Central and South American region are lacking given the small number of cancer registries that have met the data quality standards to be included in Cancer Incidence in Five Continents [21]. Statistics on incidence and mortality from HL are essential to identify disparities in cancer burden, to develop and evaluate cancer control policies and programs, as well as to guide future areas of research [22]. In this paper we describe the current burden of HL in the Central and South American region and interpret the data patterns in light of factors known to increase the risk of HL.

2. Methods

The present analysis includes Hodgkin lymphoma (C81), 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 elsewhere in this issue. In brief, we obtained regional- and national-level incidence data from 48 population-based cancer registries in 13 countries, and nationwide cancer deaths from the World Health Organization (WHO) mortality database for 18 countries. To facilitate data comparisons across countries, we used standard methods to check incidence data consistency and quality [23]. All incidence data were converted to the latest version of ICD-O (ICD-O-3) [24] and subsequently converted to the 10th edition of the International Classification of Diseases (ICD-10) [25]. Nationwide mortality data from the WHO systematically undergo data verification, and the data are coded in ICD-10 to avoid misclassification of cancer mortality over time [26]. We estimated age-standardized incidence rates (ASRs) and age-standardized mortality rates (ASMRs) per 100,000 person-years using the direct method and the World standard population [27,28]. We estimated national ASRs by aggregating the data from the available cancer registries using a weighted average of local rates. Trends in incidence were estimated for only four countries that provided written consent for the use of their data or submitted new data for about 10 years or more, and we matched mortality data to the same time-period (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. [29]. To illustrate the direction of the trends in incidence and mortality rates by cancer site, locally weighted regression (LOWESS) curves were fitted to provide smoothed lines through the scatter plot of the annual age-standardized rates by calendar period. For this report, smooth lines were computed using a bandwidth of 0.5, which means that 50% of the annual time-series data was used to determine the LOWESS plotting position for each year. 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) [30].

We present age-specific incidence and mortality patterns by country and sex. For comparative purposes, we selected the same age groups used by Hjalgrim et al. [31], except for the youngest age groups (0–14 years) where we divide the category into two (0–4 and 5–14 years) because the population in the region is relatively young [32].

We also present the distribution of HL by histological subtype, classified according to the revised WHO classification system [24] and used in Cancer Incidence in Five Continents [33].

3. Results

3.1. Age-standardized incidence and mortality rates

HL incidence rates varied 7-fold in males and 11-fold in females across Central and South America. Males generally had higher HL incidence rates than females: male-to-female (M:F) ratios ranging from 1.1 to 4.3:1.0, except in Chile (M:F ratio 1.0:1.0) (Table 2). In the most recent 5-year period, the highest incidence rates in males were observed in Argentina, Cuba, Brazil and Costa Rica (ASRs of about 2.0), whereas the lowest ASRs were in Peru, Bolivia and EL Salvador (range 0.4–0.9). Among females, the highest incidence rates were in Uruguay, Argentina and Brazil (ASRs ~1.5) and the lowest in Peru, French Guyana, Ecuador, El Salvador, and Bolivia (0.14–0.67).

Mortality rates varied 4-fold in males and 6-fold in females. Males had higher mortality than females (M:F ratios ranging from 1.1 to 2.5:1.0). Cuban males had the highest mortality rates of HL (ASMR: 1.0) followed by Costa Rica, Mexico and Venezuela (range 0.60–0.67), while the lowest were in Brazil (0.29). Females in Cuba, Costa Rica and Suriname had the highest mortality rates of HL (0.54–0.63), while Panama, Brazil, Nicaragua, Paraguay (0.13–0.20) had the lowest mortality (Table 2).

3.2. Age-specific rates

Age-specific incidence rates of HL seem to follow a bimodal pattern among males and females in most countries in the region, with the first peak seen around ages 15–24 years and the second

Table 1
Countries included in the analysis of time trends.

Country	Name 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