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Stomach cancer burden in Central and South America☆

Monica S. Sierra[a,*], Patricia Cueva[b], Luis Eduardo Bravo[c], David Forman[a]

[a] International Agency for Research on Cancer, Section of Cancer Surveillance, Lyon, France
[b] Registro Nacional de Tumores de Quito, Hospital Solón Espinosa Ayala SOLCA Núcleo de Quito, Ecuador
[c] Registro Poblacional de Cancer de Cali, Departamento de Patología, Universidad del Valle, Colombia

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ABSTRACT

Rationale and objective: Stomach cancer mortality rates in Central and South America (CSA) are among the highest in the world. We describe the current burden of stomach cancer in CSA.
Methods: We obtained regional and national-level cancer incidence data from 48 population-based registries (13 countries) and nation-wide cancer deaths from WHO's mortality database (18 countries). We estimated world population age-standardized incidence (ASR) and mortality (ASMR) rates per 100,000 and estimated annual percent change to describe time trends.
Results: Stomach cancer was among the 5 most frequently diagnosed cancers and a leading cause of cancer mortality. Between CSA countries, incidence varied by 6-fold and mortality by 5–6-fold. Males had up to 3-times higher rates than females. From 2003 to 2007, the highest ASRs were in Chile, Costa Rica, Colombia, Ecuador, Brazil and Peru (males: 19.2–29.1, females: 9.7–15.1). The highest ASMRs were in Chilean, Costa Rican, Colombian and Guatemalan males (17.4–24.6) and in Guatemalan, Ecuadorian and Peruvian females (10.5–17.1). From 1997 to 2008, incidence declined by 4% per year in Brazil, Chile and Costa Rica; mortality declined by 3–4% in Costa Rica and Chile. 60–96% of all the cancer cases were unspecified in relation to gastric sub-site but, among those specified, non-cardia cancers occurred 2–13-times more frequently than cardia cancers.
Conclusion: The variation in rates may reflect differences in the prevalence of *Helicobacter* pylori infection and other risk factors. High mortality may additionally reflect deficiencies in healthcare access. The high proportion of unspecified cases calls for improving cancer registration processes.

1. Introduction

Stomach cancer is one of the most common malignant neoplasms worldwide [1–3]. In 2012, nearly 1 million new cancer cases and 723,000 deaths were estimated to occur globally in both males and females, making stomach cancer the fifth most common cancer diagnosis (after lung, breast, colorectal and prostate cancers) and the fourth leading cause of cancer death (after lung, breast and liver cancers) [4]. More than 70% of the total number of cases occurred in less developed regions of the world (677,000 new cases and 548,000 deaths) and less than 30% of the cases occurred in more developed regions (275,000 new cases and 175,000 deaths) [4]. The age-standardized incidence rates of stomach cancer vary by 5- to 10-fold through the world, and the male-to-female ratio is 2:1 [4,5]. Eastern Asia and South America have the highest incidence rates in the world, whereas North America, Western Africa and South-Central Asia have the lowest rates [6]. Mortality rates of stomach cancer in Central and South America (CSA) are highest along the Pacific coast, with the highest mortality rates (from 12.4 to 22.3 per 100,000) in the mountains of the Andes (from Chile to Venezuela) and the Sierra Madre Mountains in Central America (from Costa Rica to southern Mexico) [7]. The worldwide variation in stomach cancer incidence and mortality rates reflect differences in the distribution of the factors associated with this disease across the world [5,8]. Moreover, stomach cancer rates, within any population, tend to be higher in those who are relatively poorer and more socioeconomically deprived [9].

* Corresponding author.
E-mail addresses: monica.sierra@alumni.uth.edu, sierram@fellows.iarc.fr (M.S. Sierra).

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The incidence and mortality of stomach cancer have been declining over the past decades in nearly all populations, regardless of the background risk of stomach cancer. The declines are thought to be due to declines in the prevalence of *Helicobacter pylori* (*H. pylori*) infection and improvements in sanitation and preservation and storage of foods and other dietary factors (high consumption of fruit and vegetables, reduced salt consumption). Changes in tobacco smoking may also play a role [8,10–12]. Despite the observed declines in incidence, the absolute burden of stomach cancer remains particularly high in several Asian and Central and South American (CSA) countries [5,8].

Although stomach cancer is usually reported as a single entity, it can be classified according to its anatomic location into cardia (CGC) and non-cardia (NCGC), and according to its histological pattern into intestinal (well-differentiated) and diffuse (undifferentiated) types [13–15]. These two classifications are currently used because their epidemiology, biology, clinical features, pathology, and precursor lesions are particular for each subtype [14–16]. Recent global estimates revealed that 87% of all stomach cancer cases diagnosed in 2012 were NCGC, with most of the cases occurring in Eastern Asia (61%) followed by Central Asia (10%), Eastern Europe (7.5%), and South America (7.0%) [3]. In 2012, the estimated incidence of CGC varied by about 3-fold in both males and females across world regions; the incidence of NCGC varied by nearly 8-fold in males and by 4.5 in females [17]. Global estimates indicate that 89% (774,000) of the NCGC cases that occurred in 2008 were attributable to *H. pylori* infection [18]. This is particularly concerning for CSA given the high prevalence of *H. pylori* infection, ranging from 50 to 95% [19–21].

Despite the reported declines in the incidence and (mainly) mortality of stomach cancer in CSA in the last few decades [1,2,12,22–28], CSA has some of the highest incidence and mortality rates in the world [4,29,30]. Recent projections indicate that the burden of stomach cancer in CSA will increase by approximately 80% by the year 2030 (102,000 new cases and 88,000 deaths); such increases are expected to be driven primarily by the growth and ageing of the population [4]. Given that the descriptive epidemiology of stomach cancer in many CSA countries is limited, we aim to describe the most current geographical and temporal trends in incidence and mortality of stomach cancer in the CSA region and present a description of the distribution of incident cases by anatomic site and histological subtype by sex. We interpret the results based on the known determinants of stomach cancer.

2. Methods

The present analysis includes stomach cancer (C16), 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 supplement (Sierra and Forman). 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 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 [31,32]. We estimated national ASRs by aggregating the data from the available cancer registries using a weighted average of local rates. To describe incidence and mortality time trends, we calculated the estimated annual percentage change (EAPC) for four countries (Table 1) using the method proposed by Esteve et al. [33]. 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 $\leq$0.05. We conducted all analyses in Stata version 12.1 (StataCorp) [34].

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

In addition, we estimated the incidence of stomach cancer by anatomic location as cardia (C16.0), non-cardia (fundus (C16.1), corpus (C16.2), antrum (C16.3), pylorus (C16.4), lesser curvature (C16.5), and greater curvature (C16.6), and other – overlapping lesions (C16.8) and unspecified (C16.9) – as classified in Cancer Incidence in Five Continents (CI5) [6]. We also evaluated the distribution of tumors by histological type [35] as intestinal (ICD-O-3 codes M8010, M8140, M8144, and M8211), diffuse (codes M8490, M8142, and M8145), and other epithelial (all other histology codes excluding M8800–M9759 and M8000–M8004) using the same classification as in other studies [36–38].

3. Results

3.1. Age-standardized incidence and mortality rates

During the most recent 5-year period evaluated, stomach cancer was one of the five most frequently diagnosed cancers in Argentina, Brazil, Bolivia, Chile, Colombia, Costa Rica, Ecuador, El Salvador, French Guyana, and Peru and one of the five leading causes of cancer death in most CSA countries (except for females in Argentina, Cuba, and Suriname). Overall, males had incidence and mortality rates 1.3–2.8 times higher than females (Table 2).

The incidence of stomach cancer varied by 6-fold across countries in CSA. In males, the highest incidence rates were observed in Chile (29.1) followed by Costa Rica, Colombia, Ecuador and Brazil, and Peru (ASRs ranging from 19.2 to 26.5) while the lowest rates were observed in Mexico, Bolivia and El Salvador (3.3–4.6). In females, the highest ASRs were seen in Peru, Costa Rica, Ecuador, Colombia, Chile and Brazil (9.7–15.1) and the lowest rates were in Mexico, Bolivia and El Salvador (ASRs $\leq$3.0) (Table 2).

Mortality rates of stomach cancer varied by 5–6-fold in CSA. In males, the highest mortality rates were observed in Chile and Costa Rica (ASMRs: 20.1–24.6) followed by Colombia and Guatemala (17.4–17.8) and the lowest rates were in Suriname, Cuba and Paraguay (5.0–7.1). In females, the highest ASMRs were seen in Guatemala (17.1) followed by Ecuador and Peru (10.5–11.2) and the lowest rates were in Paraguay, Argentina, Cuba and Suriname (2.9–3.9) (Table 2).

3.2. Age-specific rates

Stomach cancer incidence and mortality were strongly related to age. In the majority of CSA countries, 80–97% of all the stomach cancer cases were diagnosed in older men and older women ($\geq$50 years) and 3–18% were diagnosed in younger men and women ($<$50 years) in the most recent 5-year period. In Bolivia and Mexico, 21% and 19% of the cases, respectively, were diagnosed in younger men. In French Guyana, El Salvador, Mexico, and Costa Rica 20–25% of the cases were diagnosed in younger women. The mean age at diagnosis across CSA countries ranged from 61 to 68 years in males and from 59 to 73 years in females (data not shown).

Incidence rates slowly increase after age 40–44 years and gradually increase with advanced age, reaching a peak around age $\geq$75 years (Figs. 1 and 2). Stomach cancer mortality rates followed a