Parasite Epidemiology and Control 1 (2016) 56–65

Contents lists available at ScienceDirect

Parasite Epidemiology and Control

journal homepage: www.elsevier.com/locate/parepi

Trends and spatial patterns of mortality related to neglected tropical diseases in Brazil

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ARTICLE INFO

Article history:
Received 29 December 2015
Accepted 2 March 2016
Available online 7 April 2016

Keywords:
Neglected tropical diseases
Time trend analysis
Spatial analysis
Epidemiology
Mortality
Brazil

ABSTRACT

We analysed nationwide trends and spatial distribution of NTD-related mortality in Brazil. We included all death certificates in Brazil from 2000 to 2011, in which NTDs were recorded as any causes of death. A total of 100,814/12,491,280 (0.81%) death certificates were identified, which mentioned at least one NTD. Age-adjusted NTD-related mortality rates showed a significant decrease over time (annual percent change [APC]: −2.1%; 95% CI: −2.8 to −1.3), with decreasing mortality rates in the Southeast, South, and Central-West regions, stability in the Northeast region, and increase in the North region. We identified spatial and spatiotemporal high-risk clusters for NTD-related mortality in all regions, with a major cluster covering a wide geographic range in central Brazil. Despite nationwide decrease of NTD-related mortality in the observation period, regional differences remain, with increasing mortality trends especially in the socioeconomically disadvantaged regions of the country. The existence of clearly defined high-risk areas for NTD-related deaths reinforces the need for integrated prevention and control measures in areas with highest disease burden.

1. Introduction

Despite receiving more and more attention by clinicians, policy makers and the scientific community, Neglected tropical diseases (NTDs) continue being an important cause of morbidity and mortality in endemic countries, perpetuating the vicious cycle of poverty (WHO, 2010; Hotez et al., 2011).

Brazil – a country of continental dimensions with a population of about 200 million – is particularly affected, and has recently been considered to be a "hot spot" for NTDs (Hotez, 2014). In fact, 13 of the 17 NTDs are present in its territory (Martins-Melo et al., 2016a), with the largest numbers on the American continent of cases of leprosy, trachoma, schistosomiasis, leishmaniasis, soil-transmitted helminth infections, dengue fever, filariasis and Chagas Disease (Hotez, 2008; Hotez and Fujiwara, 2014).

We have recently described the epidemiological characteristics of NTD-related mortality over a period of 12 years, considering the underlying cause of death (Martins-Melo et al., 2016a). While the analysis of underlying causes of death is usually applied as

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http://dx.doi.org/10.1016/j.parepi.2016.03.002

standard, an analysis of multiple causes of death (i.e. underlying and associated causes of death) will facilitate trend and spatial analyses, besides the inclusion of information on NTDs that are usually not selected as an underlying cause of death (Martins-Melo et al., 2012a, 2015a, 2014a, 2016b). Knowledge of the geographical distribution and trends of NTD-related deaths in endemic countries is essential for monitoring and evaluation of the impact of disease prevention and control intervention strategies, and the effectiveness of disease-specific control measures (Martins-Melo et al., 2012a, 2014a, 2014b). As the NTD burden differs by Brazilian regions, with most diseases occurring in areas of low socioeconomic status, mainly in the North and Northeast regions (Hotez, 2008; Hotez and Fujiwara, 2014; Lindoso and Lindoso, 2009), and as there have been particular characteristics of occurrence over time, we here present a trend and spatial analysis of NTD-related mortality in Brazil from 2000 to 2011, based on multiple causes of death.

2. Material and methods

2.1. Study design and population

We analysed nationwide temporal trends, spatial and spatiotemporal high-risk clusters of NTD-related mortality. We included all deaths in Brazil between 2000 and 2011, in which NTDs were mentioned on death certificates, either as underlying or as associated causes of death (multiple causes of death). We selected all NTDs as defined by the World Health Organization, regardless if there are autochthonous cases reported or not (Martins-Melo et al., 2016a, WHO, 2010, 2013, 2014a). We used the Tenth Revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) for coding causes of death (WHO, 2014b).

2.2. Data sources

Mortality data were obtained from death certificates, as available from the Mortality Information System (*Sistema de Informação sobre Mortalidade — SIM*) of the Brazilian Ministry of Health. Death certificates include information on sex, age, education, ethnicity, marital status, date of death, place of residence, place of occurrence of death, and causes of death. The data are public domain (Ministério da Saúde do Brasil, Departamento de Informática do Sistema Único de Saúde, 2014). Details on downloading and processing the roughly 12.5 million data sets have been described previously in detail (Martins-Melo et al., 2016a, 2012a, 2015a, 2012b).

Census data were obtained from the Brazilian Institute of Geography and Statistics (*Instituto Brasileiro de Geografia e Estatística — IBGE*) — we used exact information for 2000 an 2010 (years of demographic censuses in Brazil), and estimates for inter-census years (2001–2009, and 2011) (Instituto Brasileiro de Geografia e Estatística (IBGE), 2014).

2.3. Data analysis

Crude and age-adjusted NTD-related mortality rates (per 100,000 inhabitants) and their associated 95% confidence intervals (CIs) are presented for the overall population and subgroups. Age-standardized rates were calculated by applying the direct method (Brazilian 2010 census as standard population).

As shown previously by our group (Martins-Melo et al., 2016a), the great majority of NTD-related deaths was associated with Chagas disease. Thus, we analysed separately deaths excluding Chagas disease, in addition to the analysis of all NTD-related deaths.

2.3.1. Trend analysis

Time trend analysis of age-adjusted mortality rates was performed using joinpoint regression models (Kim et al., 2000), stratified by region of residence. Details of the analysis have been described previously (Martins-Melo et al., 2015a, 2014a, 2014b). Statistical significance was tested using the Monte Carlo permutation test (Kim et al., 2000). The annual percent change (APC) and 95% CI are presented for each segment to describe and quantify the trend, and to assess significance (Kim et al., 2000).

2.3.2. Descriptive spatial analysis

We analysed the spatial distribution and spatial–temporal patterns of mortality using municipalities as the geographical units of analysis ($n = 5565$; Brazilian territorial division of 2010). We first calculated the average annual crude mortality rates (per 100.000 inhabitants) by municipality. To correct for random fluctuations and to provide greater stability of mortality rates mainly in small municipalities, we calculated smoothed mortality rates by applying the Local Empirical Bayesian smoothing method (Assunção et al., 1998).

2.3.3. Spatial cluster analysis

We evaluated the presence of global spatial autocorrelation using Global Moran's I index (Cliff and Ord, 1981). To identify significant spatial hot spots, cold spots and outliers (high values surrounded by low values or low values surrounded by high values) of mortality rates, we assessed local autocorrelation (Local Index of Spatial Association — LISA) by means of Local Moran's I index (Anselin, 1995). For spatial representation of the Local Moran's index, Moran Maps were used considering municipalities with statistically significant differences ($p < 0.05$).