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Trends in schistosomiasis-related mortality in Brazil, 2000–2011

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ABSTRACT

Schistosomiasis is an important public health problem, with high morbidity and mortality in endemic countries. We analysed the epidemiological characteristics and time trends of schistosomiasis-related mortality in Brazil. We performed a nationwide study based on official mortality data obtained from the Brazilian Mortality Information System. We included all deaths in Brazil between 2000 and 2011, in which schistosomiasis was mentioned on the death certificate as an underlying or associated cause of death (multiple causes of death). We calculated crude and age-adjusted mortality rates (per 100,000 inhabitants), and proportional mortality rates. Trends over time were assessed using joinpoint regression models. Over the 12-year study period, 12,491,280 deaths were recorded in Brazil. Schistosomiasis was mentioned in 8,756 deaths, including in 6,319 (72.2%) as an underlying cause and in 2,437 (27.8%) as an associated cause. The average annual age-adjusted mortality rate was 0.49 deaths/100,000 inhabitants (95% confidence interval: 0.46–0.52) and proportional mortality rate was 0.070% (95% confidence interval: 0.069–0.072). Males (0.53 deaths/100,000 inhabitants), those aged ⩾70 years (3.41 deaths/100,000 inhabitants), those of brown race/colour (0.44 deaths/100,000 inhabitants), and residents in the Northeast region of Brazil (1.19 deaths/100,000 inhabitants) had the highest schistosomiasis-related death rates. Age-adjusted mortality rates showed a significant decrease at a national level (Annual Percent Change: −2.8%; 95% confidence interval: −4.2 to −2.4) during the studied period. We observed decreasing mortality rates in the Northeast (Annual Percent Change: −2.5%; 95% confidence interval: −4.2 to −0.8), Southeast (Annual Percent Change: −2.2%; 95% confidence interval: −3.6 to −0.9), and Central-West (Annual Percent Change: −7.9%; 95% confidence interval: −11.3 to −4.3) regions, while the rates remained stable in the North and South regions. Despite the reduced mortality, schistosomiasis is still a neglected cause of death in Brazil, with considerable regional differences. Sustainable control measures should focus on increased coverage, and intensified and tailored control measures, to prevent the occurrence of severe forms of schistosomiasis and associated deaths.

1. Introduction

Schistosomiasis (or Bilharzia) is a parasitic disease caused by trematode worms of the genus *Schistosoma* (the main species that cause human infections are *Schistosoma mansoni*, *Schistosoma haematobium* and *Schistosoma japonicum*) (Gryseels et al., 2006; Raso et al., 2007; World Health Organization, 2013, 2014). Schistosomiasis is one of the Neglected Tropical Diseases (NTDs) (World Health Organization, 2013), and is the second most important socio-economically devastating parasitic infection after malaria (Chitsulo et al., 2000). The disease is intimately associated with poverty and poor socioeconomic conditions in many regions of the world, especially in places without access to clean water and with poor sanitation (Raso et al., 2007; World Health Organization, 2014).

The disease is considered endemic in 78 countries in Africa, the Americas, the Middle East, and southeastern Asia (World Health Organization, 2013, 2014). It is estimated that approximately 200–250 million people are infected worldwide (Steinmann

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et al., 2006; World Health Organization, 2014), with 600–780 million at risk of infection (Steinmann et al., 2006; Clements et al., 2008; World Health Organization, 2014), and 200,000–280,000 deaths are attributed to the disease annually (Van der Werf et al., 2003; Steinmann et al., 2006). Most infected people live in sub-Saharan Africa (Steinmann et al., 2006; Clements et al., 2008; World Health Organization, 2013, 2014).

In Brazil (and in all other American endemic countries), schistosomiasis is caused by *S. mansoni*, and the intermediate hosts are snails of the genus *Biomphalaria* (*Biomphalaria straminea*, *Biomphalaria glabrata* and *Biomphalaria tenagophila*) (Brazilian Ministry of Health, 2012; World Health Organization, 2014). Schistosomiasis has an extensive transmission area in Brazil, with endemic and focal areas encompassing 19 of the 27 federative units/states (Brazilian Ministry of Health, 2012). Its occurrence is focal and directly linked to the presence of snail intermediate hosts (Coura and Amaral, 2004). The most heavily affected areas are characterised by poor sanitary conditions, poverty and low education levels, especially in states of the Northeast and Southeast regions (Brazilian Ministry of Health, 2012). It is estimated that approximately 2.5 to 6 million people are infected (5–10% may develop severe hepatosplenic and potentially fatal forms), and 25 million who live in endemic areas are at risk of infection (Katz and Peixoto, 2000; Brazilian Ministry of Health, 2012). Between 1990 and 2010, a significant number of severe forms was recorded, with an average of 1,567 annual hospitalizations and 527 deaths (Brazilian Ministry of Health, 2012).

The Brazilian Schistosomiasis Control Program (Programa de Controle da Esquistossomose, PCE) bases its control actions on diagnosis and timely treatment of infected people, with diagnosis through stool surveys in endemic locations, with subsequent treatment dictated by the percentage of individuals positive for infection in the surveyed area (Brazilian Ministry of Health, 2010, 2012; Nascimento and de Oliveira, 2014). The prevention of the occurrence of severe forms of schistosomiasis and deaths is one of the aims of the schistosomiasis control and surveillance programs in Brazil (Silveira et al., 1990; Amaral et al., 2006; Brazilian Ministry of Health, 2012; Nascimento and de Oliveira, 2014). Thus, knowledge of the burden and dynamics of schistosomiasis-related deaths in Brazil is essential to monitor and evaluate the impact and effectiveness of the control measures in reducing infection prevalence and the occurrence of severe forms of the disease (Silveira et al., 1990; Resendes et al., 2005; Amaral et al., 2006; Ferreira and Tabosa, 2007; Nascimento and de Oliveira, 2014). In this nationwide study, we analysed the epidemiological characteristics and temporal trends of schistosomiasis-related mortality in Brazil, during the years 2000 to 2011.

2. Material and methods

2.1. Study area

Brazil covers a total territory of 8.5 million km^2 and had an estimated population of 201 million people in 2013. It is divided into five geographic regions (South, Southeast, Central-West, North and Northeast), 27 Federative Units (26 states and one Federal District), and 5,570 municipalities (Instituto Brasileiro de Geografia e Estatística (IBGE); http://www.ibge.gov.br).

2.2. Study design and population

We performed a time series study based on secondary national mortality data. We included all deaths in Brazil between 2000 and 2011 (the latest year with available and compiled data in January 2014), in which schistosomiasis was mentioned on death certificates, either as an underlying or as an associated cause of death (for so-called multiple causes of death). Since 1999, the Brazilian Mortality Information System (Sistema de Informação sobre Mortalidade, SIM) has provided information on certificates detailing multiple causes of deaths. However, we did not include 1999 in the analysis, as during this transition period a considerable number of fields were left empty.

Schistosomiasis as a cause of death corresponded to category B65 (“Schistosomiasis (Bilharziasis)”) of the Tenth Revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) (World Health Organization, 2010).

2.3. Data sources

Mortality data were obtained from the SIM, Brazilian Ministry of Health. SIM data are in the public domain and freely available at the website of the Informatics Department of the Unified Health System (Departamento de Informática do Sistema Único de Saúde (DATASUS), http://tabnet.datasus.gov.br/cgi/sim/dados/cid10_indice.htm). SIM data are based on death certificates, consisting of a standardised form to be completed by physicians and which contains socio-demographic and clinical information (causes of death). We processed a total of 324 mortality data sets, with approximately 12.5 million entries. Details on downloading of the data sets and data processing of SIM databases have been described previously (Martins-Melo et al., 2012a,b).

Population data for the period were obtained from the IBGE, based on the Brazilian Population Censuses (2000 and 2010) and population estimates for inter-census years (2001–2009 and 2011) (IBGE; http://tabnet.datasus.gov.br/cgi/deftohtm.exe?ibge/cnv/popuf.def).

2.4. Statistical analysis

Variables available on death certificates include: sex, age, race/colour, marital status, place of residence or occurrence of death, and underlying or associated cause of death. Descriptive statistics for the study population included the calculation of means and S.D. for continuous variables and absolute numbers and proportions (with their respective 95% confidence intervals (95% CIs)) for categorical variables.

Crude mortality rates (with their 95% CIs) by sex, age group, race/colour and place of residence (macro-regions and federative units/states) were calculated by dividing the number of deaths related to schistosomiasis in each calendar year by the population, and expressed per 100,000 inhabitants. Age-adjusted rates and the 95% CIs were calculated by the direct method, using the Brazilian population of the 2010 Census as the standard. Age categories employed in standardization and calculation of age-specific mortality rates were: 0–14, 15–29, 30–39, 40–49, 50–59, 60–69 and $\geqslant$ 70 years. Based on the mortality rates, relative risks (RR) and the 95% CIs were estimated to determine differences among study groups (sex, age groups, geographic regions of Brazil, and race/colour group). We also calculated the proportional mortality rates, stratified by place of residence (macro-regions and states), by dividing the number of deaths related to schistosomiasis by the total number of deaths, and multiplied by 100.

Time trends were assessed by joinpoint regression analyses to provide the annual percent change (APC) in mortality rates and to identify points where a statistically significant change over time in the linear slope of the trend had occurred (Kim et al., 2000). Time trends were calculated using age-standardised rates (sex and the five geographic regions of Brazil), age-specific rates and proportional mortality rates (for the five geographic regions of Brazil) as dependent variables and the year of occurrence as an independent variable. Joinpoint regression analysis identified joinpoints via a log-linear method, where the direction or the