The Burden of Chagas Disease

Estimates and Challenges

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ABSTRACT

Chagas disease, caused by infection with the protozoa *Trypanosoma cruzi* is transmitted most often by Triatominae insect vectors, but also through blood transfusion, organ transplant, and congenital transmission. Between 5 and 18 million people are currently infected and the infection is estimated to cause more than 10,000 deaths annually. The disease has 3 phases: acute, indeterminate, and chronic. The acute phase immediately follows infection. It is typically asymptomatic but produces fever and malaise in up to 5% of people. The indeterminate phase is asymptomatic. More than one-half of those infected will remain in this phase for life and never experience long-term sequelae. After a decade or more, 20% to 30% of people will experience chronic cardiovascular Chagas disease with sequelae including heart failure, arrhythmias, and thromboembolism. Another 15% to 20% will experience chronic digestive sequela including megaesophagus and megacolon. A complete accounting of the burden of Chagas disease requires estimating the prevalence of the infection, the prevalence of each of its sequelae among those with the infection, and the number of deaths attributable to the infection. Attempts to estimate Chagas disease prevalence are complicated by several challenges imposed by the disease's extreme spatial heterogeneity, quickly evolving temporal trends, the decades-long lag between infection and symptomatic disease, biased prevalence data, incomplete recognition of Chagas-attributable deaths, limited data on sequela, and a near total absence of data outside of endemic countries. Even though researchers have found methodological approaches to dealing with these challenges, there is a need for better data.

Chagas disease, also known as American trypanosomiasis, is caused by infection with the protozoa, *Trypanosoma cruzi*. The infection is most commonly transmitted by Triatominae insect vectors, with members of the *Triatoma* genus being the most important transmitters, followed by members of the genera *Rhodnius* and *Panstrongylus*. Transmission to humans occurs not directly through the blood meal, but through infected feces that are deposited during the blood meal, most commonly when the bitten person rubs the infective feces into the bite wound while scratching the area. In addition to vector-borne transmission, *T. cruzi* may be transmitted through blood transfusion and organ transplantation [1]. Finally, congenital transmission occurs in approximately 5% of births to infected mothers [2].

Acute infection is typically asymptomatic, with approximately 5% of cases experiencing symptoms including malaise and fever that may last 4 to 8 weeks. Cases may experience a characteristic unilateral edema of the eyelids, called the Romaña sign, when the triatomine bite occurs near the eye. Death during the acute phase is rare, with <1 death occurring per 2,500 infections [1,3]. After this acute phase, people enter the indeterminate phase that is characterized by chronic asymptomatic infection. At least 50% of infected people will remain in the indeterminate phase for life and experience no long-term sequela. Those who go on to develop long-term sequela will typically remain in the indeterminate phase for at least 10 to 20 years. Of those infected, 20% to 30% will experience cardiac damage from the infection and, with that, develop cardiovascular sequela including heart failure, arrhythmias, and thromboembolism. Most deaths attributable to Chagas disease result from these cardiovascular sequela. Finally, 15% to 20% of cases experience digestive sequela including megaesophagus and megacolon [3,4].

The geographic distribution of Chagas disease is driven largely by the distribution of vector species, and vector-borne transmission is limited to the Americas, between 40°N and 45°S latitude, and below 1,500 m elevation [3]. Prevalence varies considerably within this area and the Pan American Health Organization's (PAHO) country-level seroprevalence estimates for 2005 range from <1 per 10,000 (0.01%) in Panama to nearly 7% in Bolivia (Fig. 1) [5]. Globally, estimates of the number of infected people range from 5 million to 18 million, with most recent research citing estimates between 8 million and 12 million [1,3,6,7]. Estimates of the number of annual deaths are less variable, ranging from 10,600 to 12,500 [8,9]. Results from the Global Burden of Disease Study suggest that, in 2010, Chagas disease was responsible for 550,000 (274,000 to 1,069,000) disability-adjusted life years (DALY), a measure that captures both premature mortality and nonfatal health loss (Fig. 2) [10].

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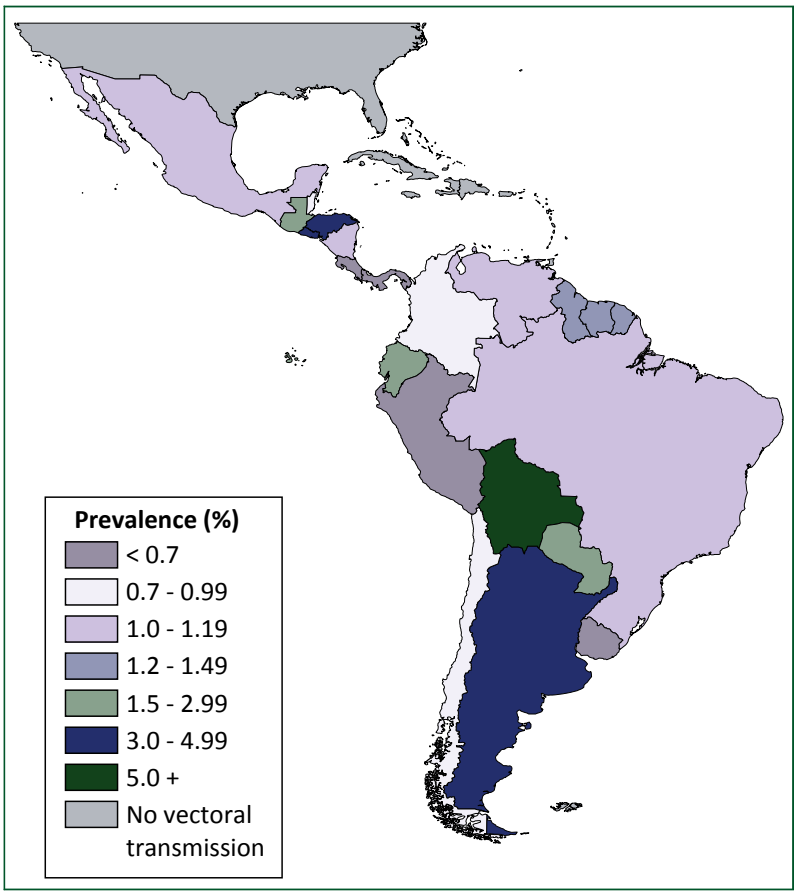

FIGURE 1. Chagas disease seroprevalence estimates for 2005 by country. Map prepared based on data from OPS/WHO/NTD/ID [5].

Control and elimination efforts have reduced incidence and shrunk the geographic limits of transmission in many parts of Latin America. Country-level ministries of health, PAHO, and the World Health Organization have coordinated 4 large-scale control initiatives for Chagas disease: the Southern Cone Initiative (launched in 1991); the Andean Initiative (launched in 1997); the Central American and Mexico Initiative (launched in 1998); and the Amazon Initiative (launched in 2004). These efforts have included education, housing improvements, insecticide spraying, and more rigorous screening of blood donors. The efforts have reduced the area and intensity of endemic vector-borne transmission throughout the region and greatly reduced transmission through blood transfusion. Globally, between 1990 and 2006, the annual number of Chagas-attributable deaths is estimated to have declined from 45,000 to 12,500; the number of new cases annually has declined from 700,000 to 41,200; and the population at risk has declined from 100 million to 28 million [9]. The Southern Cone region has experienced some of the most notable successes, and PAHO has, somewhat controversially, certified that transmission by *Triatoma infestans* was interrupted in Uruguay (in 1997), Chile (1999), and Brazil (2006) [11,12]. And while control efforts have reduced incidence in endemic countries, increased migration has expanded the geographic distribution of prevalent infections. Chagas disease is now seen among Latin American immigrant populations in North America, Europe, Australia, and Japan [6]. It is estimated that 4.2% of Chagas-related DALY and 21.7% Chagas-related health care costs now occur outside of Latin America [7].

ESTIMATING CHAGAS BURDEN: APPROACHES AND CHALLENGES

At its most basic level, estimating the burden of Chagas disease requires estimating the prevalence of the infection and the number of deaths attributable to it. A complete accounting of Chagas disease burden, however, requires estimating the frequency of symptomatic sequela of the disease, including the incidence of symptomatic acute infection and the prevalence of chronic cardiovascular and digestive sequelae. Attempts to estimate the prevalence of Chagas disease are complicated by several challenges imposed by the disease's extreme spatial heterogeneity, quickly evolving temporal trends, the decades-long lag between infection and symptomatic disease, biased prevalence data, incomplete recognition of Chagas-attributable deaths, limited data on sequela, and a near total absence of data outside of endemic countries.

Challenges in estimating prevalence

The risk of Chagas disease varies tremendously not only between countries, but also within them. Thus, community-based seroprevalence studies rarely (if ever) offer a representative view of the burden of Chagas disease for a country as a whole. Moreover, because studies tend to be preferentially conducted in communities in which Chagas disease is known to be endemic or hyperendemic, prevalence estimates from community-based studies almost universally represent a biased sample. If taken directly, results from these studies would yield dramatic overestimates of national Chagas disease prevalence. Similarly, blood donations make a convenient study sample and a number of Chagas disease seroprevalence surveys have been conducted among blood donors. The bias here tends to be the opposite of that seen in community-based studies with seroprevalence among blood donors being systematically lower than national averages. Moreover, a review of published data reveals that these biases are profound. Whereas PAHO estimated the national prevalence of Chagas disease in Brazil to be 1.02% in 2005 [5], a survey of Brazilian blood donors in that same year found a prevalence of only 0.15% [13], and a community based study in Porto Letícia, São Paulo, reported a prevalence of 5.6% [14]. Studies have typically used some means of statistical correction to account for these known biases. In some cases, investigators have conducted meta-analyses of community-based studies to develop estimates of prevalence among those living in endemic areas and then adjusted these estimates downward based on the