Chagas disease in Latin America

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Chagas is a neglected tropical disease that is endemic to various countries in Latin America and has infected up to eight million people, a majority of whom are unaware they are even infected (CDC, 2022). This disease was discovered by Carlos Ribeiro Chagas, a Brazilian doctor, in 1909 and since then Latin America has begun to intensify its reports of the disease (Lidani et al., 2019). There is an annual average incidence of 30,000 new cases, 12,000 deaths, and around 9,000 newborns infected through gestation (PAHO/WHO). This disease is spread in many ways, such as through congenital transmission, blood transfusions, organ transplantations, and consumption of contaminated food and water (CDC, 2022). However, the most common way that individuals are infected is through vector-borne transmission, by an insect only found in the Americas (CDC, 2022). This insect is called the triatomine bug, widely known as the kissing bug. It can transmit Chagas to humans by passing on the parasite Trypanosoma cruzi through its feces, which is the causative agent of the disease (CDC, 2022). When the feces of the infected triatomine bug enters the body through broken skin or through the unintentional introduction of the feces to the eyes, nose, or mouth, the person becomes infected with the parasite and will enter the acute phase of the disease (PAHO/WHO). During the acute phase, the disease can be cured, and patients are typically treated with antiparasitic drugs such as benznidazole (CDC, 2022). However, due to the acute phase commonly being asymptomatic, those infected are left undiagnosed and progress to the chronic phase of the disease (PAHO/WHO). This latter phase of the disease can last an entire lifetime and is associated with cardiac and gastrointestinal complications in up to 30% of infected individuals (CDC, 2022). Although the causative agent and the threat of leaving individuals infected with Trypanosoma cruzi have been established, more attention needs to be directed toward preventing the transmission of Chagas disease and improving treatment methods to prevent future unnecessary deaths and infections in Latin America.

Lack of education on Chagas disease

One of the main contributors to the continued uncontrolled spread of Chagas is the lack of education on the disease and its vector by both the public and physicians. Physicians from Yucatan, Mexico, which is an endemic region, displayed a gap in knowledge regarding the general facts about the disease such as diagnostics, treatment, and even transmission of the disease(Lugo-Caballero et al., 2017). Trypanosoma cruzi was identified as the causative agent of Chagas disease by 77% of doctors, however, 68% believe that the disease is only transmitted via a vector (Lugo-Caballero et al., 2017). As mentioned, Chagas disease has multiple modes of transmission and is not exclusive to vector-borne transmission, displaying physicians' lack of education on how the disease can spread. Seventy-eight point six percent of physicians stated that they would suspect Chagas if a patient presented symptoms such as an edematous lesion on the eyelids, but only 40% of the participating doctors in this study indicated the proper diagnostic method, which is either a PCR or an immunosorbent assay (Lugo-Caballero et al., 2017). Physicians cannot even identify proper diagnostic methods, making it extremely difficult for them to administer proper treatment since they are unable to properly determine if people even have Chagas disease.

Not only are physicians undereducated about the disease, but the public is undereducated as well. In one study, individuals from various rural and urban regions in Bolivia were asked about their perception and knowledge of the triatomine bug. Indigenous populations such as Ayoreo and Guarani were more aware of the triatomine bugs than individuals who lived in an urban setting (Salm & Gertsch, 2019). Unexpectedly, however, the indigenous populations were less educated on the bugs than the urban populations were. Specifically, in Ayoreo, only about 24% knew about Chagas disease, 4% did not consider the disease dangerous, and 12% simply considered the bugs a nuisance (Salm & Gertsch, 2019). Although people in Ayoreo were able to identify the bugs, few of them were able to associate them with the life-threatening disease and were unafraid of the bugs themselves. The other rural populations stated that they had heard of a disease associated with the bug but were unable to name the disease that it caused (Salm & Gertsch, 2019). Their lack of education on Chagas disease and how it is transmitted to humans via the triatomine bug feces creates a lack of threat perception since they are not educated on the danger of the disease. The gap in education on Chagas disease in both the public and physicians makes it extremely difficult for measures to be taken for both prevention and treatment of the disease and inevitably causes avoidable complications and deaths.

Cultural impact on Chagas disease

Minimal education on Chagas disease is not the only contributor to its prevalence in Latin America, but cultural aspects in various countries have impacted its prevalence as well. Foods, such as various fruits consumed in Brazilian and Venezuelan culture, are often contaminated with triatomine feces, making them vehicles for the oral transmission of Chagas disease, which is slowly becoming the most frequent mode of transmission (Nascimento et al., 2021). A major suspect in the transmission of Trypanosoma cruzi is the açai berry, which is commonly consumed as a beverage in Latin America (Santana et al., 2019). In Brazil, between 2007 and 2016, there were 1,579 confirmed cases of acute Chagas disease in Pará (Nascimento et al., 2021). Nascimento et al. analyzed the prevalence of the disease in the Tocantins health region of Para, where they had the highest concentration of confirmed disease cases. In the Tocantins health region, there is an abundance of açai production and consumption, due to the fruit being a large part of their culture and their economy (Nascimento et al., 2021). Açai production is a major source of their income and is also a large part of their diet, often considered by the locals as their main meal (Nascimento et al., 2021). They found that many of the acute cases of Chagas were confirmed between the months of July and December, which correlated with the harvest time of açai (Nascimento et al., 2021). To confirm if these cases were spread through the consumption of açai, they determined the modes of infection and discovered that 73.59% of the cases were transmitted orally (Nascimento et al., 2021). Santana et al. also conducted a study in Brazil where they confirmed that individuals who had consumed açai from the same source tested positive for Trypanosoma cruzi. Similarly, in Venezuela, there was an outbreak of orally transmitted Chagas in 2009, and the culprits were the artisanal juices that were being prepared and served at the local school in Chichirivivhe de la Costa (Alarcón de Noya et al., 2016). Information on whether infected and uninfected individuals consumed artisanal juices from various fruits such as guava, melon, passionfruit, and papaya juice were obtained and 100% of individuals who were infected with the parasite had consumed some type of juice (Alarcón de Noya et al., 2016). Of those that were infected, 73.5% of them consumed guava juice, suggesting that guava was the central vehicle of the transmission of the disease (Alarcón de Noya et al., 2016). Oral transmission of Chagas disease through contaminated foods, such as açai and guava, has been associated with more severe cases of the disease causing a rapid evolution to complications such as myocarditis and higher morbidity (Miranda-Arboleda et al., 2021). This emphasizes the importance of directing efforts to educate people on the transmission of Chagas and the need to administer food sanitation regulations to prevent the further spread of Chagas through oral transmission.

Chagas disease social impact

Variables such as socioeconomic and social status have also presented challenges in Chagas disease treatment and prevention. Chagas disease is widely considered to be a disease limited to poverty-ridden regions in Latin America (Jimeno et al., 2021). This is because they have scarce resources and vector control regulations were either not implemented or maintained in these regions (Jimeno et al., 2021). Both creoles and Qom live in poverty within the highly endemic region of Pampa del Indio in the Argentine Chaco (Fernández et al., 2019). The Qom, however, were associated with a higher social vulnerability index, meaning that they had lower levels of education, lower economic status, poorer housing conditions, and far less access to sanitation and healthcare than creoles (Fernández et al., 2019). A higher social vulnerability index was associated with much higher levels of Trypanosoma cruzi infested homes and higher levels of infection (Fernández et al., 2019). The higher

rate of infection and infestation is due to their housing conditions, which consist of mud walls and cardboard walls and roofs, making them more vulnerable to triatomine bugs (Fernández et al., 2019). Their low levels of vector control through their lack of insecticide use are also a huge contributor to the high rates of home infestations (Fernández et al., 2019). Creoles, who had a lower social vulnerability index, were twice as likely to use insecticides, proving that vector control methods are less likely to be maintained in more socially vulnerable populations (Fernández et al., 2019). Overall,populations of higher social vulnerability index are subject to higher infection and infestation rates, revealing that inequalities in healthcare are based on different social and economic statuses. This is key to assessing what populations in Latin America need to be targeted for vector control, case detection, and treatment of Chagas (Fernández et al., 2019). It will also aid in lowering the rates of infection, spread, and health inequalities among different social and economic statuses.

Chagas disease economic impact

Chagas disease also heavily impacts the economy in Latin America. It has caused a loss of 752,000 days (about 2,059 years) of work and has an average annual cost of $1.2 billion in the southern regions of Latin America (Miranda-Arboleda et al., 2021). It is estimated that an infected person from low to middle-income countries in Latin America faces upwards of $636 in annual health expenses (Olivera & Buitrago, 2019). Specifically in Colombia, around 788,742 adults are predicted to have Chagas disease, which makes up 1.6% of their population (Olivera & Buitrago, 2019). However, only 1.2% of the predicted cases know that they have the disease (Olivera & Buitrago, 2019). From just that small percentage of individuals, it accumulated a total direct medical cost of US $5.7 million, which is 53.2% of the total medical costs in Colombia in 2017 (Olivera & Buitrago, 2019). This economic burden is due to the cardiac complications associated with Chagas that require expensive diagnostic tests, specialized medical consultations, and implantation procedures (Olivera & Buitrago, 2019). Had all the individuals been diagnosed with Chagas disease, the direct medical expenses would have surpassed US $140 million, which would have placed Colombia in a much more detrimental economic state (Olivera & Buitrago, 2019). The indirect medical costs attributed to Chagas disease was US $5.8 million and its main contributor was presenteeism (Olivera & Buitrago, 2019). Presenteeism is known as decreased work performance due to illness, and it accounted for more than 50% of the indirect costs of Chagas (Olivera & Buitrago, 2019).

Premature mortality because of Chagas disease has also heavily impacted the economy due to lost productivity in Colombia. In 2017 it contributed US $515,228 to the total indirect costs, which is minuscule in comparison to the cost of presenteeism (Olivera & Buitrago, 2019). However, it has heavily contributed to the cost of lost productivity (Olivera & Buitrago, 2019). From 2010 to 2017, there were 1,261 deaths from Chagas disease at the working age, which added up to a total of 48,621 potential years of work lost (Olivera et al., 2021). The total cost of lost productivity from premature mortality was US $29,683,913 (Olivera et al., 2021). Fifty-eight percentof the total cost was attributed to men because a higher percentage of them died and they have higher wages and employment rates than women (Olivera et al., 2021). The cost per age group was also evaluated, and they discovered that the mean age of premature death was 21, which is part of the younger working population (Olivera et al., 2021). This means that premature deaths were from the younger populations, and the economic costs of their death were much higher than those of the older population. The cost of their deaths from 2010 to 2017 was on average US $3 million annually, which was significantly higher than the average of US $77,000 in the older age group (Olivera et al., 2021). Had there been an implementation of Chagas disease detection and treatment, it is likely that this economic burden on Columbia from the complications and deaths of the disease could have been easily avoided.

Chagas disease treatment

Despite Chagas disease having a major negative impact on the economy and the lives of Latin Americans, there is limited treatment. Currently, there are only two drugs, created in the 70s, that treat Chagas disease: benznidazole and nifurtimox (Pinheiro et al., 2017). However, nifurtimox was discontinued in Brazil, Argentina, Chile, and Uruguay because of its high toxicity during the 80s (Ribeiro et al., 2020). It is now only used when benznidazole is ineffective and even then, requires authorization from WHO to be used (Ribeiro et al., 2020). The treatment options for Chagas disease are already limited, and with nifurtimox being discontinued, there are even fewer ways to cure the acute phase of the disease. In addition to this, benznidazole is only manufactured by the Pharmaceutical Laboratory of the State of Pernambuco, in Brazil, and a private laboratory in Argentina because there is an inflated cost of production (Ribeiro et al., 2020). Since the one drug that can be used to treat Chagas is only produced in two laboratories in Latin America, there is limited supply and access to them. Benznidazole also has negative side effects in up to 40% of patients and has recently been found to have no effect on patients with Chagas-related cardiomyopathy (Beaumier et al., 2016). Since it is unable to help with cardiomyopathy, it proves only effective during the acute stage of the disease, which stresses the need to administer treatment to patients with Chagas in a timely and efficient manner. However, patients are rarely diagnosed during the acute stage, and patients infected with Trypanosoma cruzi that have been diagnosed are not prescribed the drug if they are considered clinically well, despite a multitude of different studies stating that if all infected patients are administered benznidazole it can prevent the progression of the disease into the chronic phase (Pinheiro et al., 2017). The expansion of benznidazole in all Chagas patients will help lower the prevalence of the disease and the rate of morbidity.

Given the challenges associated with the current form of treatment, it is crucial that new, safer, effective, and more affordable forms of treatment be developed. There has been a lack of incentive for companies to develop new treatments such as possible new drugs and even vaccines because the disease is associated exclusively with those living in poverty (Beaumier et al., 2016). Although expensive and time-consuming, in recent years there has been work done to try and develop a new drug. These drugs are being tested and are still in the pre-clinical stage, but many of them have been found to have some effect on Trypanosoma cruzi (Ribeiro et al., 2020). However, they have not been tested for long enough to determine exactly how the parasite has been affected (Ribeiro et al., 2020). The most effective synthetic drug being studied is the compound GNF6702, which has been found to inhibit some biological components of the parasite without affecting human components in any way (Ribeiro et al., 2020). Not only are new drugs being developed, but a vaccine is being made as well. There are two vaccine profiles, prophylactic and therapeutic, that could, respectively, help prevent acute infections and those that are already infected with the parasite (Beaumier et al., 2016). There have been trials using recombinant proteins and viral vectors, as well as DNA platforms that have proven to be effective in protecting against infection in animal models (Beaumier et al., 2016). It is estimated that if an effective vaccine from these trials is developed for humans, it can prevent cardiac complications as well as lower mortality rates in children (Beaumier et al., 2016).

The therapeutic Chagas disease vaccine can be used on pregnant women to prevent congenital transmission and has been estimated to have an extremely positive impact on the Latin American economy (Bartsch et al., 2020). In Latin America, up to 40% of pregnant women are infected with Trypanosoma cruzi, resulting in congenital transmission of Chagas disease (Bartsch et al., 2020). Infected children can develop severe Chagas disease symptoms and 6.5% of the cases result in death (Bartsch et al., 2020). It is extremely difficult to diagnose an infant with Chagas disease because the process for diagnosis in infants is much more complicated and they must go through various testing that can take up to a year to complete (Bartsch et al., 2020). This leaves many infants undiagnosed and untreated, resulting in up to a 30% chance of them developing the chronic form of the disease (Bartsch et al., 2020). Benznidazole is not recommended for pregnant women, so the development of a vaccine is a viable way to terminate the spread of Chagas disease through congenital transmission (Bartsch et al., 2020). With the development of a 75% efficacious vaccine, it is estimated that 375 congenital cases per 10,000 Trypanosoma cruzi infected pregnant women will be averted (Bartsch et al., 2020). Additionally, this will also reduce the number of infants that progress to the chronic stage of the disease (Bartsch et al., 2020). As a result, it is predicted to save thousands of dollars because fewer infants will have to go through different forms of costly testing and treatment (Bartsch et al., 2020). Depending on the various efficacy levels of the vaccine, it can save US $42,487 to US $131,452, from a third-party payer perspective and US $403,083

have thousands of dollars because fewer infants will have to go through different forms of costly testing and treatment (Bartsch et al., 2020). Depending on the various efficacy levels of the vaccine, it can save US $42,487 to US $131,452, from a third-party payer perspective and US $403,083 to US $1.22 million from a societal standpoint (Bartsch et al., 2020). The development of a vaccine for Chagas disease is a promising solution to terminate the spread of Chagas disease through congenital transmission because of its ability to prevent the suffering of both mother and child whilst saving thousands of dollars from both a societal and economic standpoint.

Chagas disease interventions

Although the development of new forms of treatment will be extremely beneficial in lowering the rate of morbidity and advancement of Chagas disease into the chronic stage, there needs to be an implementation of different interventions to improve the care of patients and to control the spread. As previously mentioned, physicians lack sufficient knowledge about Chagas disease, hindering their ability to accurately diagnose and provide proper treatment for infected patients. The addition of online training courses about Chagas disease can prove to be extremely beneficial in educating physicians about the disease. This is because an online training course can reach more people than a traditional in-person class would (Gurgel-Gonçalves, 2022). An online training course would make learning about Chagas more accessible, and it is extremely important in maintaining the visibility of Chagas disease and will strengthen health professionals' abilities to treat and diagnose patients (Gurgel-Gonçalves, 2022). By improving access to education about Chagas disease, physicians and even the public, will be able to learn and teach others about the disease. This will make themselves and others around them aware of the severity of the disease if left untreated and how to avoid the vector.

Moreover, eco-health interventions such as implementing window insect screens and home improvements to reduce triatomine bug infestations have proven to be extremely beneficial. In Yucatan, Mexico, members of the community came together under the coordination of social workers to build and install the insect screen in the homes of members who consented to this vector control program (Waleckx e al., 2018). A few years after the installment of the screens, it was revealed that the screens reduced the number of houses that had an indoor infestation of the triatomine bug and compared to homes without screens there was a significant difference in the number of the bugs present inside the home (Waleckx e al., 2018). This intervention has been associated with an expected 32% reduction in the yearly incidence of Trypanosoma cruzi infection (Waleckx e al., 2018). Similarly, homes in Rio Grande do Sul, Brazil, underwent changes. Before the changes, most homes in this region had wood walls, clay roofs, floor boarding, and some houses did not have septic tanks (Santos et al., 2016). These were replaced with brick walls, cement ceilings, clay tile floors, and the addition of septic tanks (Santos et al., 2016). Before these improvements, those involved in the project stated that they found triatomine bugs in their homes, but after they stated they no longer saw the bugs (Santos et al., 2016). Interventions such as window screens and home improvements should be encouraged in other countries in Latin America because it is almost certain that it will lower the rate of contact with the triatomine bug, which will reduce the rate of Chagas disease infection.

There are many barriers to both the treatment and prevention of Chagas disease, which have contributed to its continued prevalence in Latin America. These barriers include a lack of education on the disease, social and economic inequalities, and cultural practices. These barriers have not only influenced the disease's spread but also negatively impacted the economy and the lives of those infected. If education on Chagas disease, increased accessibility to healthcare, and interventions such as required food sanitation and home improvements, are enforced in Latin America then these negative impacts would be reversed. Thousands would be saved from unnecessary suffering whilst also saving significant amounts of money. This is why it is important for Latin America to bring Chagas disease out of the shadows and place much more effort and funding into better treatment and preventative measures.

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