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Chagas' disease in Mexico: Factors, Surveillance, and Recommendations

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Abstract

The present work is a literature review with the purpose to analyze and discuss the key factors influencing the geographical patterns of Chagas' disease, a vector-borne, neglected tropical disease, in Mexico. Another goal is to identify surveillance and control strategies in order to decrease the burden of this disease in Mexico. One such strategy is the integrated and interdependent approach to health of humans, animals and the environment called "One Health." The literature review method using PubMed, World Cat, EBSCO, Elsevier, and WHO databases allowed to obtain relevant information for this research. A list of key words pertaining to the topic and the purpose of this work helped identify relevant peer-reviewed and other scientific articles. In addition, CDC, WHO and other gray literature documents dating from 2002 to 2015 provided up-to-date statistics and data. The literature review method revealed that health politics, domestic animals, poor housing conditions, presence of vector insects called triatomine bugs, human migration, and the screening protocol of pregnant women, blood donors, and organ donors represent the main risk factors. Also, climate change is a potential risk factor for the spread of Chagas' disease beyond the Mexican borders. Understanding these risk factors is important for health interventions, especially in surveillance and control strategies. But, surveillance and control of human health in isolation from environmental conditions, such as housing, and animal health that co-habituate with human population is not effective and sustainable. Thus, the holistic One Health approach can greatly improve surveillance and control strategies by addressing the agent-vector-host relationship and the factors that affect it.

Keywords: Chagas disease, risk factors, Mexico

1. Introduction

The ecology of any disease in a certain region is the result of many biological, geographical, and social factors constantly interacting and influencing one another. The vector-borne Chagas' disease is an emerging neglected tropical disease that is mostly distributed in Mexico and Latin America. This distribution is affected by a series of risk factors that favor the maintenance and spread of the disease in the human population. They also affect the agent-vector-host relationship by increasing the rate of contact among the three players, thus, contributing to poor health. It is important to understand the characteristics of the agent, vector, and host in order to analyze the risk factors that contribute to the actual disease distribution. Once identified, the risk factors can be used to design interventions for surveillance and control of the disease. Comprehensive interventions proved to be the most sustainable for the long-term disease control mechanisms. One such holistic approach is based on solving human health problems together with animal and environmental health issues, especially if the disease needs all these three elements in order to persist. This is called the One Health approach. Analyzing the disease ecology model for Chagas' disease, One Health approach can and should be used to eradicate the disease from human and animal populations by blocking the contact between agent, vector, and host.

1.1 The Agent

Chagas' disease, also known as American trypanosomiasis, is caused by a flagellated protozoan called *Trypanosoma cruzi*[1]. But this agent cannot infect the human host without the blood-sucking triatomine bugs. The protozoan enters the human body through infected feces of the triatomine bug rubbed against the cracked skin resulted from the bite[1]. Once in tissue, *T. cruzi* cells lose the flagellum and multiply by binary fission to form true leishmanial forms. They divide rapidly and destroy the cells of liver, spleen, lymph nodes, bone marrow and other tissues[2]. Leishmanial, crithidial and trypanosomal forms escape into the blood. Characteristic local inflammation and fibrotic capsulation occurs, which blocks the lymph capillaries causing edema or Chagoma[2]. In this way, Chagas' disease is the result of the vector-facilitated interaction between the parasite and the host.

T. cruzi is transmitted between vertebrate hosts by triatomine insect vector. The parasite is very heterogeneous and genetically diverse[3]. This parasite is ancient and has a long history of evolution. Paleomicrobiological studies on ancient populations have identified two genotypes of *T. cruzi* in humans. The type I was found about 4,500-7,000 years ago in Minas Gerais state, Brazil, which today is absent suggesting changes of time and space in the distribution pattern of *T. cruzi* genotypes in humans[3]. Today, this genotype is isolated in the Amazon Basin. The type II genotype is distributed in nature, in animal reservoirs and human hosts, causing Chagas' infections in human population[3]. *T. cruzi* reproduces in sylvatic and domestic cycles[4]. It can infect almost any tissue and more than one hundred species of mammals[3]. The existence of animal reservoirs makes the disease very hard to eradicate unless the contact between agent, vector and host is eliminated by addressing risk factors; for example, improved housing conditions and vector control programs.

1.2 The Vector

Chagas' disease is vector-borne, transmitted by triatome bugs. They are blood-sucking or haematophagous bugs from the family Reduviidae, subfamily Triatominae[5] . Because they prefer to bite on face, these bugs are called the "kissing bugs"[1, 6]. These insects exist in many species, but not all of them carry the pathogen. About 40 species of triatomes are naturally infected by *T. cruzi* in North America[1]. Of these, 28 species habituate exclusively in Mexico, and eight species are shared with the U.S.A.[1]. In Mexico, 96% of transmission of Chagas is vector-borne[1]. Interestingly, surveillance indicated that "the greatest percentage of infected triatomine bugs was observed in rural areas compared to urban areas"[1]. The numerous vector population that is found in Mexico and the existence of many species of triatomine bugs that carry the parasite increase *T. cruzi*'s potency to infect a large number of hosts.

The mechanism of infection is an important element when designing surveillance and control interventions. Chagas' disease is a vector-borne infection discovered in 1909 by the Brazilian physician Carlos Chagas. He identified triatomine bugs as the vectors for this disease[2, 6]. Also, he described that these bloodsucking insects cut the skin like razors, which explains the name "barbeiros." The triatomine bugs are sensitive to light and during the day they hide in cracks of walls and ceilings where they rest and lay eggs, but at night they become active and feed on blood of nearby sleeping humans and animals[6]. When the bug bites, it deposits feces with *Trypanosoma cruzi* that are pushed at the site of bite lesion as a result of itching. Thus, the parasites enter the bloodstream and produce the infection[3].

1.3 The Host

Chagas' disease causes a high burden on its victims. Due to genetic variability of the pathogen and host, the infection can be either acute or chronic. In severe cases, victims develop cardiomyopathy, encephalopathy, or morphologic malformations of the internal organs, and death is the final outcome[10]. The acute phase of the disease lasts for 2-4 months and occurs mostly in children[1]. The symptoms include inflammation at the inoculation site, unilateral palpebral edema, fever, muscle pain and others[1]. However, 60-70% of cases are asymptomatic[6]. About 2 to 6% of acute cases can advance by causing myocarditis and meningoencephalitis that lead to death[1]. Because the acute infection can resolve spontaneously, most of the cases are neither reported nor diagnosed. Then, the acute phase becomes chronic.

The chronic phase can last for 10-30 years or lifetime. This phase is mostly asymptomatic and no signs of disease are evident. Only the blood tests can indicate positive serology[1]. About 40% of the chronically infected people develop cardiomyopathy and up to 10 % of cases develop digestive and/or neurologic impairments[1]. Megacolon, megastomach, and megagallbladder are among the damages inflicted by the parasite to the gastrointestinal tract[1] and aneurysms and arrhythmias affect the circulatory system[7]. These conditions seriously affect the victims' normal functioning. Central and enteric nervous systems can also be harmed by the parasite *T. cruzi.* These irreversible complications increase the

morbidity and mortality rates in the endemic countries[1]. If chronically ill patients become immunocompromised due to HIV infection or organ transplant, then the disease may re-occur. In Mexico, mostly the chronic cases are reported and cardiomyopathy is diagnosed in the majority of the victims[1]. A study performed in a rural hospital in the state of Chiapas, Mexico revealed that 82.5% of cardiomyopathy cases are attributed to the chronic form of Chagas infection. Thus, the chronic infection with Chagas is the leading cause of heart failure in endemic rural and urban regions of Mexico[1]. But this burden is largely due to the fact that not all the infected people in the acute phase are aware of the infection and have sporadic access to the antiparasitic treatment.

Two available drugs, nifurtimox and benzonidazol, are used to treat the disease in the acute phase in 80% of the cases if treated early. They proved to be efficient in treating newborns contracting the infection congenitally[1, 8]. If this therapy is applied to women before pregnancy, congenital Chagas' disease transmission can be prevented. However, this therapy is useless to patients in the chronic phase[1]. Some researchers suggest that the available treatment should be used not only for the acute cases but also for the chronic infections. According to clinical and immunological evidence, all chronically ill patients should mandatorily receive the antiparasitic treatment[9]. But these drugs need more biochemical improvement in order to increase their efficiency and decrease their side effects. Making drugs available for the affected populations is important, but more efforts should be directed toward up-stream interventions mean to prevent people from getting the disease. These interventions should address the social determinants of health, including housing, poverty, migration, environment etc.

2. **Methodology**

A literature review method was applied using databases like PubMed, World Cat, EBSCO, Elsevier, and WHO to find articles containing key words such as "Chagas' disease," "risk factors," "Mexico," "surveillance," "diagnosis," "triatomine," "*Trypanosoma cruzi*," "One Health," and "climate change." In addition, Centers for Disease Control and Prevention (CDC), World Health Organization (WHO), and other gray literature documents from 2002 to 2015 were used for up-to-date statistics. Books and research articles revealed the following risk factors: poor housing conditions, human migration, health policy and diagnostic protocols, and possibly the climate change. These factors are in addition to the presence of vector, pathogen, and their interaction with the human host in the disease ecology model discussed earlier.

3. Results

The following main risk factors contribute to the current ecological distribution of Chagas' disease in Mexico: poor living conditions, health policies, human migration, and climate change. Poverty influences the living conditions. This factor contributes to the domestication of the vector bugs and intensifies the contact between the agent and the host. The domestication of triatomines and the existence of wild reservoirs in other animal species indicates the need to solve this health issue with One Health concept. In Mexico, Chagas' disease is transmitted entirely by vector; however, other ways of transmission like blood transfusion and vertical transmission have been observed. In non-endemic regions of Mexico, the disease spreads due to absence of screening tests of pregnant women and blood donors, and also due to migration of people from rural to urban regions[4]. In addition, health policies may improve the health system and delivery of care. The need for a well-functioning health system, especially in the rural areas, is reflected in the fact that early diagnosis and treatment in the acute phase can prevent a lot of suffering and disability later when the chronic phase manifests. Research showed that climate change can increase the susceptible habitat for vector population onto the United States territory, but it is not clear whether climate or migration or another factor contributes to the disease distribution toward the northern regions.

3.1 Chagas' disease and "One Health" relevance

One Health approach consist of understanding human health as interdependent on animal and environmental health. Domestic animals serve as the bridge between the human host and the agent. They can facilitate *T. cruzi* transmission by connecting wild animal reservoir to the human reservoir and by hosting the protozoan themselves. About 180 species of animals including cats, dogs, rodents, and opossums are important reservoirs and can be involved in the transmission cycle of the disease[1]. Cats and dogs are known to have a high prevalence of *T. cruzi* infection; thus, the

close presence of domestic animals can increase the risk of infection by 3 to 5 times[1]. Dogs and cats infected with *T. curzi* have been observed in Texas, U.S.A.[1]. In Mexico, some studies showed that the geographical distribution of infected domestic animals corresponded to the geographical pattern of disease based on the prevalent cases[1]. For example, in Palmar de Bravo, Puebla State, the *T. cruzi* infection showed 4% prevalence in humans and 10% prevalence in canine population[1]. The correlation between the proportion of human host infected and the animal reservoir demonstrates that the existence of domestic animal reservoirs is a risk factor for Chagas' infection and its re-occurrence in human population[1]. Given that dogs and cats are involved in maintaining Chagas transmission in rural and urban regions, these domestic animals should be included in the surveillance of the disease[1]. Also, since dogs are important reservoirs and hosts of *T. cruzi*, they can serve in animal bioassay studies to understand the mechanism of infection, the transmission of Chagas' disease, and testing of potential vaccines[1] (Carabarin-Lima et al., 2013). These strategies represent "One Health" approach and how relevant it is for Chagas' disease.

3. 2 The Burden Of Disease And Distribution

Due to its biological, ecological and social characteristics, the burden of Chagas' disease is hard to estimate. This neglected tropical disease affects mostly poor people by causing lifetime disabilities and impairments. The real burden of disease is much underestimated. In the literature, the prevalence of Chagas' disease in Americas vary between 7 million[11] and 10 million people[5]. Also, it is estimated that this disease kills annually between 14,000 people[12] and 45,000 people, mostly in Central and South America[5]. Also, a WHO report estimated 14,000 deaths in 2002, which can be translated into a burden of disease equal to about 667,000 DALYs[8]. It is estimated that about 25 million people are at risk[8]. The variation of data can be explained by the fact that Chagas' and other neglected tropical diseases affect mostly low and middle-income countries where the surveillance systems are weak, and many infected people are not diagnosed due to the lack of screening programs and poorly-equipped local medical facilities or even the absence of these in some rural regions.

In Mexico, 18 areas are endemic, almost all are rural, located mostly in southeast, and include the states of Oaxaca, Jalisco, Yucatan, Chiapas, Veracruz etc. In these regions the prevalence can exceeds 10%[1]. The highest prevalence of disease is observed in the northeastern region, which is dominated by tropical climate and includes such states as Hidalgo and Veracruz[1]. Jalisco, Oaxaca, Chiapas and Veracruz have the highest cases of Chagas disease[1]. In addition, it is estimated that each year about 243,000 fertile women in Mexico are infected with Chagas' disease, which puts about 1,100 newborns at risk of infection[1]. The regions with the highest prevalence of maternal infection such as Jalisco with 12.02% and Oaxaca with 4.4% are also with the highest prevalence of congenital transmission: in Jalisco it is 9.1% and in Oaxaca – 4.08% [1]. But these data could still underestimate the real picture of the burden it causes on people. Measurements to reduce the risk of infection with *T. cruzi* can lead toward a better quality of life for Mexican people[1].

3.3 Housing Conditions

The social aspects of Chagas' are linked to the housing conditions that greatly influence the spread of the disease in Mexico, Bolivia and other endemic countries. Thatched roofs, cracked walls, straw beds, wattle houses made of Madeira wood and scattered domestic belongings offer favorable conditions for insects to come in contact with people[4, 6]. But when public health workers or any other governmental or non-governmental entities intervene to improve the houses, they need to understand and respect them as familial and cultural institutions[6].

3. 4 Climate Change And Other Factors

Climate change is a potential factor that may spread the vector distribution of Chagas' disease toward northern regions of Mexico and into the U.S. The southern U.S. is very vulnerable to outbreaks of vector-borne diseases because of such factors as poor housing conditions, suboptimal drainage, presence of feral dogs, and human migration[5]. Triatomine species have been identified in poorly-developed areas in many states across U.S. including Texas, Florida, Arizona, Georgia, New Mexico and many others. Chagas' cases have been identified in the U.S., which occurred because of blood donors infected with *T. cruzi* from the vector[1]. In the U.S., the vector population lives in a sylvatic cycle, and the pathogen lives in animal reservoirs[1]. It is thought that animal and human habitats overlapped and the infection was transmitted to blood donors. Potent vectors have been identified in 28 states, and animal reservoirs have been found in 17 states[1]. Climate change models and scenarios indicate that climate change can increase the geographic

distribution of *T. cruzi* vector; thus, causing Chagas to emerge in areas it was absent before such as the U.S.[5]. Thus, under the scenario of climate warming in southern U.S., the triatomine population infected with *T. cruzi* would increase. However, these findings were proven for the vector expansion in the U.S. On the contrary, the main transmission route of *T. cruzi* in Mexico remains the vector.

In addition, deforestation, road construction, and land use can influence the disease ecology. Habitat change, globalization and travel can also intensify the spread of Chagas disease[5]. Climate change resulting from anthropologic events proved to shift the distribution of vector species. The distribution of the triatomine bugs depends not only on climate change but also on biological factors such as species interactions, geographic factors such as accessible regions for spreading, and anthropogenic factors[5].

Studies on ecology and biogeography of triatomines indicated shifts in the distributions of vector population and prevalence of the pathogen. According to climate models, the climate change may cause an increase of the temperature in the southern U.S., which could contribute to the expansion of vectors and high risk areas in the North America[5]. Higher temperatures can influence the behavior of triatomine species; for example, at the temperature above 30°C and low humidity, the life cycle of insects shortens causing a denser bug population and a higher frequency of bites to avoid dehydration[5].

3. 5 Surveillance and Control

Good and cost-effective surveillance and control mechanisms can stop the spreading of the disease in the environment, meaning the vector population, and animal and human populations. Solving the poverty issues and screening the blood and organ donors, pregnant women and children could improve the surveillance and evaluate the vector control programs. In addition to these interventions there are other alternatives to improve surveillance such as community-based programs.

Scholars believe that increasing awareness about Chagas' disease among young generations can increase the success rate and communities' acceptance of the control strategies. For example, research shows that community-based vector surveillance systems integrated in the primary health care services can reduce infection. A retrospective study in Honduras showed that this integrated method helped improve surveillance from 46 to 84 on a 100 point-scale. Also, risk awareness among school children increased from 77 to 83 points[13]. And the sero-prevalence declined from 3.4% to 0.4%. The health centers responded to the community bug reports by spraying the houses with insecticide[13]. Some key elements of the program were volunteers and policies. For instance, community volunteers increased the health centers' management capacity and influenced other people behaviors to report the bugs. Also, the National Chagas' Programme was essential in facilitating changes in disease distribution by assigning responsibilities, offering training, evaluating the progress, and advocating for vector control interventions[13]. But this strategy is limited by the fact that it involved only school-aged children and excluded other important stakeholders. Also, the post-intervention data represent mixed effects of spraying campaigns[13]. In addition, it requires the health care workers to engage on non-clinical activities, which creates a pressure on the personnel[13]. Nevertheless, integration of participatory modeling into the primary health care system is possible and can be successful to prevent this vector-borne infection.

4. Conclusion

The risk factors that contribute to the spatial distribution of Chagas disease and triatomine vectors in Mexico include high density of vector population, a large proportion of vectors infected with *T. cruzi*, people's migration from rural to urban areas, low socioeconomic status and poor living conditions, restricted access to trypanocidal therapy, presence of domestic animal reservoir, and the absence of screening protocols from blood and organ donors and pregnant women. Climate change was not found as a significant risk factor for the geographic pattern of disease in Mexico, but it can influence the vector distribution toward north in the U.S. Understanding these risk factors may help design cost-effective interventions in the affected communities.

Surveillance and control of human health requires a holistic approach that includes the animal health and the environmental conditions. One Health approach is recommended in order to address this disease holistically. Another approach is community-based systems integrated into the primary care services. Such surveillance approach is designed to control the vector population, increase community awareness, and education to help prevent, detect, and treat the infection while in the acute phase.

Some of the limitations of this work include the absence of results from applying One Health to surveil and control Chagas' disease in Mexico or elsewhere, the lack of strong proof that the proposed strategies could work in Mexico,

and the existence of many other obstacles in the understanding of the cultural and political realities of Mexico and those of the affected human populations. To further develop this study, it is important to analyze other strategies implemented in other countries to address the same or similar vector-borne diseases, taking into consideration the social priorities and needs of the affected populations. Among these needs may include cultural, medical, and economical. Eradication of any disease means addressing inequality and social justice.

A strong health system is detrimental to address health issues. In addition, addressing the social determinants of health should be at the core of health interventions. This is because diseases such as Chagas and other neglected tropical infections represent the tip of the iceberg called social inequality and negligence, which on the grand scale are part of global inequality.

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