Chagas Disease: seroprevalence and effectiveness of antiparasitic treatment

Enfermedad de Chagas: seroprevalencia y efectividad en el tratamiento antiparasitario

Jorge A. Monroy-Vargas [a], Eduardo Bustos-Vázquez [b], Gisela Galindo-Juárez [c]

Abstract:

INTRODUCTION: Chagas disease is considered the most serious parasitosis in America, forgotten and neglected in the world due to the limitations for its diagnosis and treatment. The objective is to evaluate the state of seropositivity of Chagas disease in Mexico and the effectiveness of the treatment in infected patients. **MATERIAL AND METHODS:** Systematic reviews were performed with searches in Crossref, Google Scholar, Scielo, PubMed and the inclusion of guides and manuals of related health programs was evaluated based on their updating and relevance. **RESULTS:** For seropositivity, the studies coincide in the characterization of the risk factors, as well as the evaluations in Blood Transfusion Centers in the country, finding captive cases in all the states. In the evidence of effectiveness, the following are presented as difficulties: the prolonged duration and the side effects, adding the lack of a reliable criterion of cure, with variations in relation to the phase of the disease (always exceeding 50%, between 1 to 30 years). **CONCLUSIONS:** Evidence on seroprevalence is scarce, however, the findings call into question the reduction in cases, and there seems to be no strict monitoring of treatments or indicators of cure in Mexico.

Keywords:

Chagas disease, seroprevalence, treatment, effectiveness, seroconversion

Resumen:

INTRODUCCIÓN: La enfermedad de Chagas es considerada la parasitosis más grave en América, olvidada y desatendida en el mundo, cuya razón radica en las limitaciones para su diagnóstico y tratamiento. El objetivo es evaluar el estado de seropositividad de la enfermedad de Chagas en México y la efectividad del tratamiento en pacientes infectados. **MATERIAL Y MÉTODOS:** Se realizaron revisiones sistemáticas con búsquedas en Crossref, Google Scholar, Scielo, PubMed y se evaluó la inclusión de guías y manuales de programas de salud relacionados con base en su actualidad y relevancia. **RESULTADOS:** Para la seropositividad los estudios coinciden en la caracterización de los factores de riesgo, así como las evaluaciones en Centros de Transfusión Sanguínea del país, encontrando casos cautivos en la totalidad de los estados. En la evidencia de la efectividad, se presentan como dificultades: la prolongada duración y los efectos secundarios, agregando la falta de criterio fidedigno de curación, con variaciones en relación a la fase de la enfermedad (siempre superando al 50%, entre 1 a 30 años). **CONCLUSIONES:** Las evidencias sobre la seroprevalencia son escasas, sin embargo, los hallazgos dejan entredicha la reducción de casos, y al parecer no existe en México seguimiento estricto de los tratamientos, ni indicadores de curación.

Palabras Clave:

Enfermedad de Chagas, seroprevalencia, tratamiento, efectividad, seroconversión

INTRODUCTION

Chagas is a life-threatening disease caused by the *Trypanosoma cruzi* parasite, which is transmitted mainly by blood-sucking vector insects (bedbugs).[1,2] American

[a] Correspondence Author: Epidemiology Department. Secretary of Health of Hidalgo, Mexico. ORCID: https://orcid.org/0000-0003-2277-5168 Email: jmv.semp10@hotmail.com

[b] Epidemiology Department. Secretary of Health of Hidalgo, Mexico. Email: edward0586@hotmail.com

[c] Epidemiology Department. Secretary of Health of Hidalgo, Mexico. Email: glgalindo@hotmail.com

trypanosomiasis is considered the most serious parasitic disease in America,[3] it is a neglected disease because of the difficulties and limitations for its diagnosis and treatment, since the interest needed to establish such strict intentional search for cases, and the effects of the treatments, the duration, without developing others, the long follow-up time and, without a doubt, the establishment of the standard criteria for a cure.[4]

Currently, *T. cruzi* infection has spread to other continents, besides Latin America, and the diagnostic capacity and follow-up of cases has become a challenge for health systems, as data on seroprevalence, understood as the general manifestation of a disease or condition within a population at any given time, measured with serological tests[5] denotes the limitations due to the epidemiological surveillance of Chagas.[6] Therefore, the main objective of the present study is to generate more precise evidence on the persistence of the disease, shown by seroprevalence and the search for the reason why the treatments established for decades without guarantee of cure are still applied.

EPIDEMIOLOGY

More than 110 years after the first observations by Dr. Carlos Chagas in Brazil, it was described by its dispersal characteristics, mainly due to the conditions of poverty and overcrowding.[2] In Mexico, the first human case was described in 1940 by Mazzotti.[7] Its dispersion occurred through internal population movements in the American continent, from the ancestral migrations of native people.[8]

According to the World Health Organization (WHO), until February 2018, it was calculated that in the world there were between 6 and 7 million people infected with *Trypanosoma cruzi*,[9] there are no accurate records; however, the figures recently published by the Department of Microbiology and Parasitology of the National Autonomous University of Mexico (UNAM), refer that it cares for approximately 10 million infected people.[10] It is found as an endemic disease in 21 Latin American countries, but in recent decades it has been observed more frequently in the United States, Canada, European countries, and some in the Western Pacific.[9]

For the American continent, it represents a major problem regarding morbidity and mortality, in addition to the disability it causes, it has become a burden that depletes the region's economic resources and affects the social and work environment of those who suffer from it. The annual incidence was registered with 28,000 cases in the region and it is estimated that it causes nearly 12,000 deaths every year.[11] Recent measurements of Chagas burden in Latin America indicate that it generates an approximate health cost of more than 500 million dollars and an annual loss of 770,000 years of life due to premature death or loss of productive years due to disability (DALYs).[4]

In Mexico, it is considered a public health problem since about 1.1 million people are infected,[12] in addition to the social, economic, and territorial conditions (social determinants), putting more than 29,500,000 at risk of contracting the infection. The National incidence rate was 0.7 per 100,000 population in 2017.[1] The state of Guerrero presented the highest rate of new cases in the acute phase. In its chronic phase, cases were registered in almost all the states, with the exception of the 2 Californias, Guerrero and Querétaro. The highest rate was observed in Yucatán (3.96). In 2018, the entities with the highest incidence rates were Yucatán (0.8), Quintana Roo (0.8) and Nayarit (0.7).[12]

With respect to the vector, Mexico maintains high diversity in families, 39 species have been identified and at least 21 of them have been found infected with T. cruzi.[7,13] All forms of parasite infection discovered so far must be taken in account when establishing strategies for risk surveillance and control, therefore it is crucial not to leave behind the possibilities of adaptation of triatomines.[14,15]

PHYSIOPATHOLOGY

It is a parasitic tissue and blood disorder.[16] When the infected vector feeds, it can ingest and defecate on the skin or mucous membranes of the mammal, by doing so, it deposits, together with its excrement, infectious metacyclic trypomastigotes.[17] The entrance doors for these infectious parasitic forms are also opened by other mechanisms such as: blood transfusion, organ transplant, congenital (vertical) route, laboratory accidents (handling of samples and bedbugs), and by ingestion (orally),[6] the latter has taken great interest in current studies in South America since contamination of food and beverages increases the risk of becoming infected.[18]

Once the parasites have entered the host's cells through one of the possible mechanisms, it completes more than one replication cycle, to then freely pass into the bloodstream. In this stage, the parasite is able to overcome the host's immune responses, where they end up being lodged in the spleen, liver and/or cardiac tissue. The main damage is characterized by the invasion of cells, the replication and release of new parasites, leading to cell death, and consequently localized inflammation and direct injury to the tissues where it has been housed.[17]

Chagas symptoms can vary in severity, depending on the exposure or the type of transmission:

1) Acute phase: the first signs appear at least a week after the parasitic invasion (3 to 10 days from the incubation period) and parasites can be found in the blood circulation within 4 to 6 months after infection.[17] When the microorganism penetrates through a laceration of the skin, it causes an edema, called chogoma.[19] Romana's signs appear when the bite has occurred near the face or directly in the eyelid making this a sign of acute disease.

The patient presents fever, malaise, anorexia, and edema of the face and lower extremities. It is often accompanied by generalized lymphadenopathy, hepatosplenomegaly, and CNS abnormalities. After four to eight weeks, the acute signs and symptoms disappear spontaneously.[19]

2) Subclinical phase (undetermined): it is silent and can last up to 20 years before presenting damage characteristic of the chronic phase. During this period, isolated electrocardiographic changes (arrhythmias and tachycardias) can appear and in some cases sudden death can occur without apparent cause. The presence of circulating parasites is rare.[17]

3) Chronic phase: it manifests itself several years or even decades after the initial infection, frequently covers the heart, and the symptoms are due to rhythm disturbances, cardiomyopathy and thromboembolism. It causes heart failure due to atrophy of the walls when the parasite lodges in the heart muscle. Patients with megaesophagus suffer from dysphagia, odynophagia, chest pain, and regurgitation. Patients with megacolon suffer from abdominal pain and chronic constipation, which predispose them to the formation of fecalomas. The advanced megacolon generates obstruction, volvulus, sepsis, and death. It is estimated that 30% of infected people develop the chronic phase.[17,19]

DIAGNOSIS

In endemic areas, establishing the suspicion or clinical diagnosis of Chagas, compared to suggestive symptoms of Chagas in its different stages, is very rare,[4] and many of the places where cases occur come from areas in which the contact with the units is essentially at the first level of care. Consequently, among other reasons, the few training and information that doctors and health personnel receive on these issues, generates passive epidemiological surveillance. Evidence of this is the large proportion of cases that are diagnosed by the Blood Transfusion Centers (CTS) upon user demand and that are also detected in the chronic stage. For example, during the period 2000-2012, 5, 463 Chagas cases were processed, of which 247 were acute, 171 chronic with symptoms, and 5,045 chronic without symptoms.[4]

Because *T. cruzi* is in the bloodstream during the acute phase, laboratory techniques rely on the use of blood samples to detect it.[17] In Mexico, there is a network of laboratories that carry out the application of a series of inter-direct methods that include: microscopic fresco observation, concentration method, PCR and mainly the thick drop technique,[20] almost always applied only when the operational definition based technically on the clinical identification of the common sign of the phase (sign of Romagna-Mazza). In order to make a diagnosis in the indeterminate and chronic phase, it is feasible to apply indirect serological methods since there is a low level of parasitaemia and high levels of IgG,[1] the most commonly used are: indirect hemagglutination, the ELISA test,

immunofluorescence (IFI) and immunodetection on solid supports (Western Blot).[20] However, it is ideal to take as a reference Table 1.

TREATMENT

It is important to note that, in general, control programs orient the strategies towards the vector, leaving the infected patient in the background. So that 110 years after its discovery, the ideal treatment is not yet available.[6]

Table 1. *Interpretation of results for Chagas disease.*

Symptomatology	Presence of parasites	Two serological test	Case classification
Meet definition of suspicious acute case	+	-	Acute case confirmed
Meet definition of suspicious acute case	+	+	Acute case confirmed
Meet definition of suspicious acute case	-	+	Acute case confirmed
Meet definition of suspicious chronic case	-	+	Asymptomatic chronic case
Meet definition of suspicious chronic case	+	+	Asymptomatic chronic case
Meet definition of suspicious chronic case	-	+	Symptomatic chronic case
Meet definition of suspicious chronic case	+	+	Symptomatic chronic case
Meet definition of suspicious chronic case	-	-	Case discarded

Source: Undersecretariat of Health Prevention and Promotion. Ministry of Health in Mexico, 2015.

Although the treatment is recommended precisely for all people who have received a diagnosis of acute, congenital infection and for those with depressed immune systems, as well as for all children and adults with chronic phase infection;[21] however, contraindications due to the high rate of side effects keep pregnant women, patients over 75 years of age out of the possibility of receiving treatment, cases with impossibility of follow-up such as frequent change of address, kidney or liver failure, severe or uncontrolled comorbidities, neurological diseases, severe digestive symptoms, chronic Chagas' heart disease and indication for pacemaker implantation.[1]

The treatment has two main objectives:

1) Primary: eliminate the parasite and contribute to reducing the probability of developing the clinical manifestations of the disease and its complications.

2) Secondary: contribute to the disruption of the *T. cruzi* transmission chain.[1]

But, currently there are only two specific antiparasitic drugs approved for treatment, both are controlled by the Secretary of Health in Mexico and do not exist commercially in any country, since there is strict control in the distribution of these drugs by certified providers, for example, they are only available in the United States through the Centers for Disease Control and Prevention (CDC).[16,21] Nifurtimox and Benznidazole, with a duration of 60 to 90 days respectively, certain conditions and characteristics of the case. Despite the establishment of treatment there are multiple obstacles such as: the availability of the drug, lack of pediatric presentation (for Nifurtimox, the donation by the Pan American Health Organization [PAHO] does not cosider it), lack of resources for diagnosis and follow-up, lack of trained specialists to provide care, etc.[22] However, manufacturers of anti-chagasic drugs are not interested in meeting the necessary requirements to include Benznidazole in the Basic Health Sector chart.[13]

Since 1960, both drugs have been available, with the aim of being supplied from the acute phase of the disease, since they are effective in extracellular forms.[6] Both drugs have adverse side effects, mainly in the first 3 weeks after starting treatment, among a considerable percentage of patients who present from digestive, cutaneous, neuromuscular and hematological reactions, from mild, moderate and severe presentations, with children having the best tolerance compared to adults and, since long periods of treatment with an uncertain efficacy are required, the patient chooses abandonment.[6,23]

Therefore, it is necessary to review the effectiveness, understood as the capacity of the treatments, through monitoring, to comply with the cure standard, either by verifying the presence of parasites in the body or by anti-T cruzi antibodies. In Mexico, current epidemiological surveillance has not documented and yielded data regarding strict follow-up and cure for confirmed patients. It is a long-term process, where abandonment of treatment, migration, passive surveillance, and access to health services are crucial.

MATERIAL AND METHODS
Rapid systematic reviews were conducted to obtain information based on field studies to generate a more accurate assessment of the status of seropositivity and the effectiveness of Chagas disease treatments. Crossref, Google Scholar, Scielo, PubMed were reviewes, and the inclusion of guides and manuals for health programs related to the subject were evaluated in this paper based on their content, updating and relevance. Regarding the terms for the search and selection were: "Chagas disease", "seropositivity", "treatment", "effectiveness" and "seroconversion". For the selection by type of studies, the following were taken into account: cross-sectional studies to verify seroprevalence in the population without prior diagnosis, Cohort and experimental studies to verify the effectiveness of the recommended chagasic treatments.

The date proposed as a reference for the topicality of the articles will be publications from the year 1960, referring to the inclusion of the drugs of choice (Nifurtimox and Benznidazol); limiting those publications in the Spanish language.

RESULTS
Seroprevalence in Mexico
Five cross-sectional studies applied in different places of the Mexican territory, without prior diagnosis, evaluated seropositivity in humans and triatomines, with the characteristics of coinciding social determinants (type of dwelling, overcrowding, type of community, antecedent of entomological identification), as well as in Blood Transfusion Centers (CTS) of the country, with high prevalence rates in each of the sectors studied. The ages most affected with the infection range from 18 to 80 years old, as has been shown in the literature; in addition, although the articles do not show significant differences in terms of sex, with respect to the occupation of people with Chagas disease, women dedicated to the home presented a higher percentage of affectation, also associated with factors that have been gaining more force in studies carried out in America, such as the material of the houses, where there are cracks and coexistence with animals, which must have access to the interior of the dwellings, confirming that the greatest probability of contamination is vectorial when sleeping next to the walls, data shown in Table 2.

In the most recent years, results were issued on an 11-year longitudinal study to monitor seroprevalence in the case of the 516 Blood Transfusion Centers, of which the following stood out: private (46%), Ministry of Health (19%), IMSS (13%), ISSSTE (9%), State Services (5%), PEMEX (3%), University Hospitals (2%), Red Cross (1.1%), SEDENA (0.6%), DIF (0.8%) and the Secretary of the Navy (0.6%). In the study, each year there was a record of donor seropositivity, highlighting cases in all the states of Mexico.[12,20]

Treatment effectiveness
Regarding the evaluation of the effectiveness of the treatment of choice for Chagas disease, four reviews were included, where the long duration and side effects are presented as difficulties of the etiological therapy, adding the lack of a reliable criterion for cure, mainly in chronic cases. For some researchers, serological conversion is an indication of cure, this only happens in 60-75% of acute acquired cases and in 100% of congenital acute cases, and in chronic cases many times 20 to 30 years after the end of therapy and in most cases, patients die before this happens; however there is evidence of

the reappearance of the circulation of parasites in the body (Table 3).[15,22]

Considering the data from two manuals of procedure for diagnosis and treatment in Mexico, the action of currently existing drugs has proven to be very effective in the acute phase, where serological reconversion usually occurs in a short time (up to 1 year). In chronic patients, seroconversion can occur much later (10-15 years). In the acute phase the efficacy is variable but always higher than 60%. In the undetermined chronic phase the efficacy is around 60% and in the symptomatic chronic phase the efficacy of the treatment could vary around 10% and 25% in terms of serological reconversion.[1,20] In the study carried out as a systematic review by PAHO, treatment outcomes in different conditions were analyzed, with certainty of the studies between low and medium, according to its GRADE scale (for its acronym in English Grading of Recommendations Assessment, Development and Evaluation) to provide greater credibility and scientific guarantee.[4]

Table 2. *Seroprevalence studies in Mexico.*

Study name	Sample	Diagnostic method	Main findings
1. Description of the Chagas disease in Valle de Iguala, Guerrero, Mexico, 2003.	3 municipalities of the Iguala Valley, Guerrero: 450 individuals and 82 homes.	ELISA, BIORad protein concentration, Antibodies: latex agglutination, Xenodiagnosis, Echocardiogram.	Prevalence: 1.78%; 2 of the 3 municipalities with seropositivity (1.94% -1.96%); Ages: 30-80 years. Transmitter: *Triatoma Pallidipennis* (adult stage), 32.4% infected with *T. cruzi*, 100% of the locations.
2. Epidemiology of Chagas disease in the state of Veracruz, 2005.	281 rural locations, 2,526 homes, 9,782 individuals (9 of 11 health jurisdictions).	Direct hemagglutination (HAI) (+ ≥1: 16) (- ≤1: 8), ELISA (+ ≥0.200 OD). In case of 1 positive of the above, it was applied: Indirect immunofluorescence (IFI) (+ ≥1: 32).	People: 624 positive to 1 or 2 tests; 392 serum confirmation (63 positive 2 of 3 tests); 33 positive to 3 tests; prevalence of 0.1% - 2.8%; Ages: over 19 years. Entomological indices: 13.5%; 100% infestation index at all stages of the vector, natural infection of 10.6% (11: 100 infected with *T. cruzi*). Domiciled transmitter: *Triatoma dimidiata*: intradomiciled (89%), and peridomicile (11%); ectopes: bedroom (84%); distribution: wall-bed (56%), bed (39%), floor (4%), wardrobe and window (1%).
3. Prevalence of seropositivity to T. cruzi in Hidalgo: some characteristics of the homes and living with domestic animals. 2006.	84 municipalities: 1,607 individuals	ELISA	132 positive individuals: prevalence of 8.21%
4. Seroprevalence of Chagas disease in Tamazunchale, San Luis Potosí, 2009.	734 participants	Direct hemagglutination (HAI) (+≥1: 8).	Prevalence: 6.3% (n = 46), average age of 31.6
5. Manual of Procedures for Chagas disease in Mexico. 2019.	Human donors (2007-2017)	Direct hemagglutination (HAI), ELISA, Indirect immunofluorescence (IFI).	2007: 54.1% of samples from the Blood Transfusion Centers, and gradually a higher percentage, up to 100% of the samples analyzed in 2017. Annual constant seroprevalence of 0.4% to 0.37% (2007-2017). 2017: 100% of states of the republic with seroprevalences, national average of 0.37 per 100 studied.

Source: Own elaboration, 2020.

Table 3. *Effectiveness of chagasic treatments.*

Study name	Main findings	Conclusions
1. To treat or not to treat? The scientific controversy about the treatment for chronic patients of Chagas. 2010.	- 1965: clinical evaluation of Nifurtimox (Brazil, Chile and Argentina). High seroconversion rates in acute cases, with discrepancy in Brazil due to the persistence of antibodies. 1977 and 1978, in the case of Benznidazole: high rates of chronic phase healing with the criterion of elimination of the parasite in blood. - 1983-1991: Ministry of Health and the WHO in the face of uncertainty, excluded treatment for chronic phase, overlapping the criteria of cure by serology. - 1994: WHO publishes a significant decrease in antibodies in late chronic patients compared to the untreated group; during long-term follow-up (more than five years) the antibodies disappeared within 10 to 20 years. Criticism for lack of validity criteria (MBE standards).	1998: WHO establishes the starting criteria for treatment from 15 years of age, by medical criteria, until now there are controversies and results of studies are expected (TREANA and BENEFIT).
2. Trypanocidal drugs for chronic asymptomatic infection with Trypanosoma cruzi. 2008.	- Minimum abandonment due to side effects of Benznidazole and with Itraconazole due to the duration of treatment. - Incidence of changes in the ECG was very low (OR = 0.41), with ELISA the probabilities changed (10.91 to 22.33 times more for OR) and for xenodiagnostic it was with significant changes (OR = 5.37). - Substantial differences from those treated with Benznidazole and Nifurtimox (OR = 31.44) compared to those treated with Itraconazole and Alopurinol, by xenodiagnosis. - There were no estimated changes regarding the determination of seroconversion (5 children out of 44 with benznidazole, 2 of 44 with placebo).	Inconclusive results.
3. Current state of the Chagas disease treatment. 2011.	- Acute phase: with Nifurtimox and Benznidazole, 70 to 75%, which increases to 100% in congenital cases. In chronic phase: 30%. - With Itraconazole: 20% of cases with parasitological cure but without seroconversion and 50% of electrocardiographic improvement in chronic symptomatic phase. - Chronic cases: the post-treatment cure between 20 and 30 years later.	In recent studies in animals infected with *T. cruzi* and cured animals that did not present parasites or antigens of T. cruzi, they had central memory CD8 lymphocytes that maintained a positive serology for more than a year.
4. Serological and parasitological evolution post-treatment of patients with recent chronic Chagas disease. 2006.	- 5 children in a row: 100% conversion to parasitemia (negative, from baseline, 1, 2, 5 and 10 years post-treatment), but with the presence of anti *T. cruzi* antibodies, mainly in the first 3 measurements (basal, 1, 2 and 5 years, finding only a negative case at 10 years for IgG in both ELISA and IFI).	When the follow-up of patients treated in the chronic phase of Chagas disease is done for a sufficiently long time, no negative conversion of serology is observed in the first years but in much longer periods of 10 to 20 years.

| 5. Guide for diagnosis and treatment of the Chagas disease. 2018. | - Acute phase: 151 participants, 20-month follow-up, probability of negativizing 25.5 times with treatment. At 1 year in different studies with multiple methods, seroconversion in 89% with Benznidazole and 73% with Nifurtimox, while in the congenital form it was 50% and 60% respectively, determined with xenodiagnostic.
- Adults in undetermined phase: 1.98 times more likely to negativize, with post-treatment PCR; 3.32 times more for seroconversion between 2 and 3 years post-treatment; In pediatric patients, seroconversion occurs with a probability of 2.41 times more post-treatment between 2 and 3 years.
- Adults in chronic phase: 1.98 times more likely to negativize with PCR in the post-treatment. | It was recommended to perform serological tests for people discarded for donation to find risk factors. |

Source: own elaboration, 2020.

DISCUSSION

Despite the fact that in some studies considerations regarding socio-economic, demographic, cultural factors, and coexistence with animals have been omitted, positive cases were found in the populations approached without prior medical diagnosis.[5,26,28] Some factors increase the risk more than others, because they facilitate the infestation and permanence of triatomines, and therefore the host-vector interrelation, such as the coexistence with dogs and cats, which represents a food source for triatomes.[25] It should be considered that the use of pyrethroid insecticides as an action to cut this chain and eliminate the triatomine, has been proven that they do not manage to finish the bed bug with full effectiveness, but they achieve irritation forcing it to leave the cracks;[26] however the ability to fly and adapt to different habitats, when leaving these hostilities can generate growth in its population and a vicious circle from which humans and other animals can hardly escape.

It is clear that with the active search, the findings have substantiated the existence of captive cases that mainly, as well as those that have been reported by the CTS, are in a chronic asymptomatic phase, means that the omission, the strategies of the institutions, organizations and governments for decades have permeated the redistribution of American trypanosomiasis, potentiated by social determinants.

The diagnosis in any of the phases should stop depending only on one of the clinical signs or the identification in the CTS, taking as a principle the intentional search with respect to the sum of criteria as shown in Table 1, adding the antecedent of disease in the community, ending in the constant shipment of lamellae in a random way with the portion of blood to be observed by the laboratories, as it happens with other diseases transmitted by vector.

The variability in the findings, when it comes to evaluating the effectiveness of the treatment, depends on the follow-up time, time measured in months when the treatment was done in the acute phase, in years when it was done in the early chronic phase and in decades in those treated during the late chronic phase.[29] The CTS undoubtedly represent an area of opportunity for the detection and referral of patients for their diagnosis and treatment, due to the findings frequently in the identification of risk factors and test reactivity. However, the consequences of surveillance becoming passive gives Chagas a chance to persist.[12]

Regarding the effectiveness of the treatment, it first requires more interest in the field of science, the studies are still mostly low and medium certainty; in addition, the complications for the selection on the patients have multiple variants, which form their complexity for compliance, but the importance of considering effective and reliable laboratory tests to verify the determination towards cure in the first instance, will depend on the parasitological and clinical parameters in complement, not only to demonstrate the disappearance of the circulation of parasites, but the reduction of antibodies anti *T. cruzi*. There is no convincing evidence if this happens in humans, but if so it would explain the phenomenon of parasitological cure in chronic cases without serological conversion.[30] It is necessary to take into account that the monitoring of the disappearance of the indicators of cure and physiological alterations of the disease must be continuous in at least 12 years to make it effective, since the reactivation of the disease is also a fact with consequences that cause serious problems to multiple organs.

CONCLUSIONS

The persistence of the disease undoubtedly depends entirely on the factors considered in the social determinants and on the epidemiological surveillance established for the disease. The monitoring of the effectiveness of the treatment, the identification of possible adverse effects to the anti-Chagas

drugs, in addition to the development of the resistance of the parasite, are aspects of surveillance that need to be strengthened. he Mexican health system currently has the

challenge of analyzing the rehabilitation of the platform and strengthen its strategies to cut the Chagas transmission chain.

REFERENCES

1. Centro Nacional de Programas Preventivos y Control de Enfermedades. Manual de diagnóstico y tratamiento de la enfermedad de Chagas. [Document on internet]. 2015. [Update 2020; cited February 15, 2020]. Available in: https://www.gob.mx/salud/documentos/manual-de-diagnostico-y-tratamiento-de-la-enfermedad-de-chagas

2. Salazar-Schettino PM, Bucio-Torres MI, Cabrera-Bravo M, de Alba-Alvarado MC, Castillo-Saldaña DR, Zenteno-Galindo EA, et al. Enfermedad de Chagas en México. Rev. Fac. Med. UNAM. 2016; 59(3). 6-16.

3. Guadalupe Pérez SM, Hernández Meléndez E, Rodríguez Cabrera A. La enfermedad de Chagas como un rezago social en salud. Rev. Cub. Salud Pública. 2011; 37(1): 159-74.

4. Organización Panamericana de la Salud. Guía para el diagnóstico y el tratamiento de la enfermedad de Chagas. [Document on internet]. 2018 [Update 2020; cited February 11, 2020]. Available in: http://iris.paho.org/xmlui/bitstream/handle/123456789/49653/9789275320433_spa.pdf?sequence=5&isAllowed=y

5. InfoSIDA. Glosario: seroprevalencia. [Document on internet]. 2020. [Update 2020; cited February 11, 2020]. Available in: https://infosida.nih.gov/understanding-hiv-aids/glossary/1326/seroprevalencia

6. Guzmán Marín E, Acosta-Viana KY, Jiménez-Coello M. La enfermedad de Chagas: retos del tratamiento. Rev. Biom. 2016; 27(3): 95-8.

7. Instituto de Diagnóstico y Referencia Epidemiológicos "Dr. Manuel Martínez Báez". Lineamientos para la vigilancia epidemiológica de Chagas por laboratorio. México, 2015; versión 01: 1-52.

8. Pinto Dias JC. Tendencias sociales de la enfermedad de Chagas para las próximas décadas. Salud Colectiva. 2012; 9(1): 39-47.

9. Organización Mundial de la Salud. Enfermedad de Chagas (tripanosomiasis americana). [Document on internet]. 2018 [Update 2020; February 13, 2020] Available in: https://www.who.int/es/news-room/fact-sheets/detail/chagas-disease-(american-trypanosomiasis)

10. López P. La enfermedad de Chagas, silenciosa y potencialmente mortal. Gac. UNAM. 2019; (5): 118.

11. Álvarez-Hernández DA, Franyuti-Kelly GA, Díaz-López R, González-Chávez AM, González-Hermosillo-Cornejo D, Vázquez-López R. Chagas disease: Current perpectives on a forgotten disease. Rev Méd Hosp Gen Méx. 2018; 81(3): 154-164.

12. Rojo-Medina J, Ruiz-Matus C, Salazar-Schettino PM, González-Roldán JF. Enfermedad de Chagas en México. Gac Médica México. 2018; 154: 605-12.

13. Secretaría de Salud. Programa de Acción Específico, Prevención y control de la enfermedad de Chagas 2013-2018. Programa Sectorial de Salud. [Document on internet]. 2013. [Update 2020; cited February 15, 2020]. Available in: http://www.cenaprece.salud.gob.mx/descargas/pdf/PAE_PrevencionControlEnfermedadChagas2013_2018.pdf

14. Secretaría de Salud. Manual de Procedimientos Estandarizados Para la Vigilancia Epidemiológica de las Enfermedades Transmitidas por Vector. [Document on internet]. 2016. [Update 2020; cited February 15, 2020]. Available in:

http://187.191.75.115/gobmx/salud/documentos/manuales/36_Manual_ETV.pdf

15. Castillo D, Wolff M. Aspectos del comportamiento de los triatominos (Hemiptera: Reduviidae), vectores de la enfermedad de Chagas. Rev. Biom. 2000; 20: 59-64.

16. Ministerio de Salud y Protección Social, Federación Médica Colombiana 2012-2013. Enfermedad de Chagas, Memorias. [Document on internet]. 2013. [Update 2020; cited February 22, 2020] Available in https://www.minsalud.gov.co/sites/rid/Lists/BibliotecaDigital/RIDE/VS/TH/Memorias_chagas.pdf.

17. Becerril M. Parasitología Médica. In: Zavala JE, editor. Enfermedad de Chagas y otras trypanosomiasis. 4a. ed. México D.F. McGrawHill; 2014.

18. Rueda K, Trujillo JE, Carranza JC, Vallejo GA. Transmisión oral de *Trypanosoma cruzi*: una nueva situación epidemiológica de la enfermedad de Chagas en Colombia y otros países suramericanos. Rev. Biom. 2014; 34: 631-41.

19. Longo D, Kasper D, Jameson L, Fauci A, Hauser S, Loscalzo J. Harrison Principios de medicina interna. Cap 213 Enfermedad de Chagas. 18va. ed. Vol. 2. México D.F. McGrawHill; 2012.

20. Secretaría de Salud. Manual de Procedimientos para la Enfermedad de Chagas en México. [Document on internet]. 2019. [Update 2020; cited February 23, 2020]. Available in: https://www.gob.mx/cms/uploads/attachment/file/447946/Manual_de_Procedimientos_para_la_Enfermedad_de_Chagas_en_Mexico.pdf

21. Centros para el Control y Prevención de Enfermedades. Enfermedad de Chagas. [Document on internet]. 2016. [Update 2020; cited February 23, 2020]. Available in: https://www.cdc.gov/parasites/chagas/es/tratamiento.html

22. Werner APT B, Zulantay I. Estado actual en el tratamiento de la enfermedad de Chagas. Rev. Med. Chile. 2011; 139: 247-57.

23. Belaunzarán M. Enfermedad de Chagas: globalización y nuevas esperanzas para su cura. Rev. Argent. Microb. 2015; 47 (2): 85-7.

24. Becerril-Flores MA, Valle-De La Cruz A. Descripción de la enfermedad de Chagas en el Valle de Iguala Guerrero, México. Gac. Méd. Méx. 2003; 139(6): 539-34.

25. Grupo de Estudio sobre la enfermedad de Chagas, Segura E L, Escobar-Mesa A. Epidemiología de la enfermedad de Chagas en el estado de Veracruz. Rev. Salud Pública Méx. 2005; 47(3): 201-8.

26. Gómez Gómez JV, Muñoz Juárez S, Ortiz Espinoza RM. Prevalencia de seropositividad a *T. cruzi* en Hidalgo: algunas características de las viviendas y la convivencia con animales domésticos. Rev. Fac. Med. UNAM. 2006; 49(5): 190-3.

27. Aldana Cruz O, Escobedo de la Pena J, Velasco Castrejón O, Guzmán Bracho C. Seroprevalencia de la enfermedad de Chagas en Tamazunchale San Luis Potosí. Enf Inf Microbiol. 2009; 29(3): 107-10.

28. Carrillo-Peraza JR, Manrique-Saide P, Rodríguez-Buenfil JC, Escobedo-Ortegón JF, Rodríguez-Vivas RI, Bolio-González ME, Barrera-Pérez M, Reyes-Novelo E, Sauri-Arceo CH. Estudio serológico de la Tripanosomiasis Americana y factores asociados en perros de una comunidad rural de Yucatán, México. Arch. Med. Vet. 2014; 46: 75-81.

29. Vera de Bilbao N, Elías E, Martínez J, Carpinelli de Tomassone M, Torres S, Sosa L, Díaz V. Evolución serológica y parasitológica post-tratamiento en pacientes con enfermedad de Chagas crónica reciente. Mem. Inst. Investig. Cienc. Sal. 2006; 4 (1): 5-10.

30. Secretaría de Salud. Guía Metodológica de Estudios Entomológicos para Triatominos. [Document on internet]. 2015. [Update 2020; cited Frebruary 26, 2020]. Available in: https://www.gob.mx/salud/documentos/guia-metodologica-de-estudios-entomologicos-para-triatominos

31. Kreimer P, Romero LA, Bilder P. ¿Tratar o no tratar? La controversia científica sobre el tratamiento para los enfermos de Chagas crónico. Rev. Historia Medicina Ciencia. 2010; 112(2): 405-28.

    Villar JC, Villar LA, Marin-Neto JA, Ebrahim S, Yusuf S. Fármacos tripanocidas para la infección asintomática con Trypanosoma cruzi. Biblioteca Cochrane Plus. 2008; 2.