IJID Regions 12 (2024) 100410

Contents lists available at ScienceDirect

IJID Regions

journal homepage: www.elsevier.com/locate/ijregi

Short Communication

Acute Chagas disease outbreaks in Colombia in 2019

Maryi Lorena Segura-Alba[1,#], Carolina Hernandez[2,3,#], Angela Patricia Guerra[1], Nicolas Luna[2], Liliana Jazmín Cortes[1], Claudia Rincón Acevedo[1], Natalia Ballesteros[2], Martha Stella Ayala[1], Mauricio Javier Vera[4], Ricardo Andrés Caicedo Diaz[5], Susanne Carolina Ardila[6], Astrid Carolina Flórez[1], Luz H. Patiño[2], Alberto E. Paniz-Mondolfi[3], Juan David Ramírez[2,3,*]

[1] *Grupo de Parasitología, Instituto Nacional de Salud, Bogotá, Colombia*
[2] *Centro de Investigaciones en Microbiología y Biotecnología - UR (CIMBIUR), Facultad de Ciencias Naturales, Universidad del Rosario, Bogotá, Colombia*
[3] *Molecular Microbiology Laboratory, Department of Pathology, Molecular and Cell-Based Medicine, Icahn School of Medicine at Mount Sinai, New York, USA*
[4] *Subdirección de enfermedades transmisibles, Ministerio de Salud y Protección Social Bogotá, Colombia*
[5] *Drugs for Neglected Diseases initiative-Latin America, Rio de Janeiro, Brazil*
[6] *Grupo de Entomología, Instituto Nacional de Salud, Bogotá, Colombia*

ARTICLE INFO

Keywords:
Colombia
Trypanosoma cruzi
Acute Chagas disease
Oral transmission
Outbreaks

ABSTRACT

This study seeks to address the critical knowledge gap surrounding the acute phase of Chagas disease in Colombia, with a specific focus on cases reported in 2019. The acute phase of Chagas disease is a pivotal period for intervention, yet it remains poorly understood, particularly in regions where oral transmission is presumed to be a significant factor. By analyzing these recent cases, our research aims to provide a deeper understanding of the dynamics of Chagas disease during its acute phase in Colombia in 2019. This understanding is essential not only for improving disease management and treatment strategies but also for enhancing public health responses to this neglected tropical disease. In particular, our study highlights the importance of identifying and addressing the unique challenges posed by oral transmission routes, which have been increasingly recognized within Colombia's Chagas disease landscape.

Chagas disease (CD), caused by the protozoan parasite *Trypanosoma cruzi*, is primarily transmitted through the feces of infected triatomine bugs. However, oral transmission also plays a significant role, contributing to a substantial number of cases (n = 568) and outbreaks (n = 32) in Latin America. This mode of transmission is associated with a high lethality rate of 6.51%, with myocarditis leading to acute cardiac failure as the primary cause of death [1].

Oral transmission occurs when contaminated food or beverages carrying the feces of infected triatomine bugs or parasites from mammals' secretions are consumed [1]. Understanding the mechanisms and dynamics of oral transmission is crucial for scientific research, aiding in the development of effective prevention strategies and clinical management. Recognizing symptoms, early detection, and intervention during the acute phase of CD are paramount. Swift treatment at this stage can effectively prevent progression to the chronic form or death.

In Colombia, although records of isolated cases of acute CD are limited [2–4], the country has reported a significant number of outbreaks presumed to be due to oral transmission. These outbreaks have totaled 124 cases (12 outbreaks), with an 8.2% case fatality rate reported to date [1].

Serum and blood samples from 52 patients with symptoms of acute CD from February to December 2019 were studied (Table 1). Samples were collected by local health authorities and sent to the National Institute of Health (INS) for diagnostic confirmation, the national reference laboratory for public health disease surveillance. Diagnosis involved direct parasitologic tests (thin or thick blood smears, direct micro method), serological tests (enzyme-linked immunosorbent assay using total and recombinant antigens), and quantitative polymerase chain reaction (qPCR) for *T. cruzi* DNA detection and quantification (Supplementary file 1). Epidemiological investigations were conducted by INS personnel and reported in the National Public Health Surveillance System.

The study also included 15 triatomine insects and eight reservoir blood samples collected during epidemiologic investigations of two oral outbreaks. *T. cruzi* genotyping was performed as previously described [2,3]. Patient data were recorded in accordance with the official notifi-

* Corresponding author.
E-mail addresses: juand.ramirez@urosario.edu.co, juan.ramirezgonzalez@mssm.edu (J.D. Ramírez).
Maryi Lorena Segura-Alba and Carolina Hernandez contributed as first authors.

https://doi.org/10.1016/j.ijregi.2024.100410
Received 10 April 2024; Received in revised form 17 July 2024; Accepted 19 July 2024

Table 1
General epidemiological and clinical variables were included and analyzed in this study.

Transmission mechanisms	Month of occurrence	Patients confirmed									Triatomines					Host mammals				
		Department	Patients n (%)	Deaths n (%)	Direct methods n (%)	Serology n (%)	qPCR n(%)	DTU	n(% per outbreak)	Average time elapsed (symptoms onset/diagnosis)	Triatomines species	n	qPCR positive	DTU	n	Host mammals species	n	qPCR positive	DTU	n
Presumed oral transmission	May	Antioquia	3(6.5%)	0	3(100%)	1(100%)	1/1 (100%)	ND		35.3										
	May	Atlantico	3(6.5%)	1	3(100%)	3(100%)	3	ND		20.3										
	February/ March	Casanare	21(45.6%)	0	20 (95.2%)	14/14 (100%)	17/17 (100%)	TcI	9(75.0%)	18.4	*R.prolixus*	6	1(17.0%)	TcI	1	*D. marsupialis*	3	3(100%)	TcI/TcII-TcVI	3(100%)
								TcII-TcVI	1(8.3 %)		*P. geniculatus*	4	4(100%)	TcI	4	*Canis lupus*	2	3(100%)		
																			TcI	2(66.6%)
									2 (16.6 %)								3	3(100%)		3(100%)
								TcI/TcII-TcVI								*Felis catus*			TcI	
	April	Cesar	3(6.5%)	1	3(100%)	NA	NA	NA		ND										
	June	Chocó	2(4.3%)	0	3(100%)	NA	2	TcI	2(100%)	3.5										
	December	Sucre	14(30.4%)	1	12 (100%)	2 (66.6%)	5/5	TcI	4(80.0%)											
								TcII-TcVI	1(20.0%)	11.5	*R. pallescens*	5	100	TcI	5					
Vector	February to September	Casanare	5(83.3%)	0	NA	NA	5	ND		9										
	May	Meta	1(16.7%)	0	1(100%)	NA	1	ND		5										

NA, not available; ND, not detected; qPCR, quantitative polymerase chain reaction.

cation form established by INS in Colombia, and relevant variables were documented in a database (Supplementary file 2, Supplementary file 3).

Among the total reported patients (n = 52), 46 (88.5%) were linked to six outbreaks of presumptive oral transmission, whereas six (11.5%) cases involved isolated patients. The geographical distribution of patients, triatomines, and mammalian hosts involved in these outbreaks is provided. Notably, the outbreaks in Casanare and Sucre represent those with the highest number of cases, 45.6% and 30.4%, respectively (Supplementary Figure 1 and Table 1).

Among symptomatic patients, the most frequent symptoms were fever (46 patients, 88.5%), often accompanied by dyspnea (36.5%), facial edema (27.0%), and chest pain (25.0%), with overlapping symptoms (Figure 1). Less frequent symptoms (<10.0%) included hepatosplenomegaly, adenomegaly, and arrhythmia (Supplementary file 2). The Romaña sign was observed in three of six isolated cases. Regrettably, three patients passed away due to complications arising from the illness, primarily characterized by pericardial effusion and heart failure (Supplementary file 2). The time intervals between symptom onset and death varied, with durations of 22, 4, and 15 days, respectively.

Most cases (50, 96.2%) were confirmed by direct methods (thick blood smears and/or direct micro method), complemented by qPCR and serologic tests (Table 1). Molecular analyses were conducted on a subset of 34 samples, all of which were positive, revealing an average parasitic load of 27.1 parasite equivalents/mL determined through qPCR. Regarding molecular characterization, the TcI discrete typing unit (DTU) was predominant, accounting for 66.6% of cases, followed by TcII-TcIV (9.6%) and mixed infection TcI/TcII-TcIV (23.8%). Serologic tests were used to confirm the diagnosis in 21 (40.3%) cases, of which 20 (95.3%) were positive.

Epidemiologic investigations conducted by health authorities took place during two significant outbreaks in Casanare and Sucre (Table 1). These investigations involved collection of triatomines and mammalian blood samples, with all secondary vectors (*Panstrongylus geniculatus* and *Rhodnius pallescens*) testing positive for TcI infection (Table 1). In addition, during the Casanare outbreak, mixed DTU infections were observed in patients and *Didelphis* (Table 1).

Diagnosing acute CD is highly challenging due to its varied clinical presentation, which overlaps with many other infectious illnesses. From 2017 to 2022, 146 cases were reported, with 36.0% occurring in 2019. Outbreaks linked to oral transmission accounted for 46 cases. Factors contributing to this increase include: (i) integration of CD into Public Health Surveillance [5], (ii) vector control programs targeting *R. prolixus* may have inadvertently increased oral transmissions by secondary vectors [5], and (iii) collaborative efforts improved diagnostic and surveillance capabilities.

In addition, a noteworthy observation is that 80% (five of six) of oral outbreaks occurred during periods of low precipitation (Table 1, Supplementary file 2). Drought conditions, global warming, and habitat fragmentation induce the movement of wild mammals and secondary vectors from forest environments to domestic settings, thereby facilitating vector invasion and food contamination in human settlements [2,6]. This phenomenon has been extensively documented as the probable cause of oral outbreaks in Brazil, Colombia, and Venezuela [2,6].

Diagnosis predominantly relied on direct tests, highlighting enhanced local diagnostic capabilities and proficient parasite identification in clinical laboratories. The median parasitic load in our study surpassed that reported for patients with acute CD in Colombia [2,3] but remained lower than cases documented in Venezuela and Brazil [1]. In addition, we observed a high concordance (>95.0%) between the diagnostic methods used (direct methods, qPCR, and serology) for detecting *T. cruzi* during the acute phase of CD. This, combined with reduced time from symptom onset to diagnosis (Table 1), signifies increased awareness among medical professionals in suspecting CD in the presence of nonspecific symptoms because specific and severe symptoms such as hepatosplenomegaly and adenomegaly were observed less frequently.

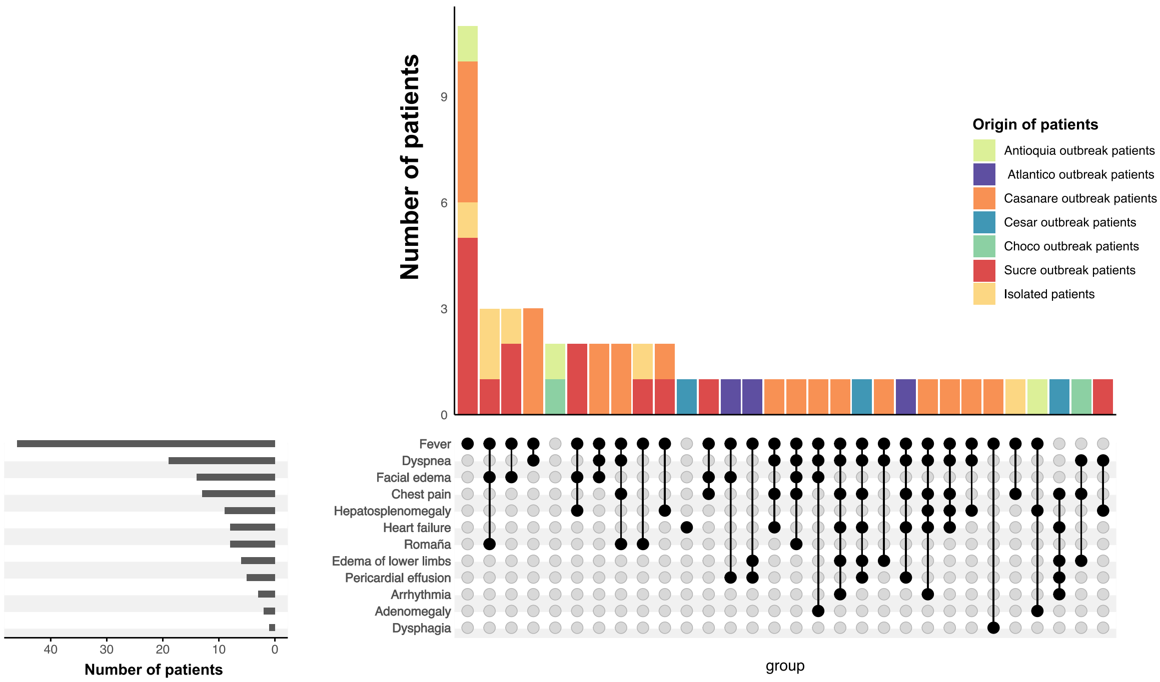

Figure 1. Symptoms of outbreaks and isolated patients. Number of patients with acute phase symptoms in each outbreak and isolated patients.

Our analysis of specimens obtained from *P. geniculatus* and *R. pallescens*, both associated with oral transmission outbreaks in the Orinoco [2] and Atlantic regions [7], respectively, is detailed in Table 1. This suggests the need for implementing targeted vector control and surveillance initiatives specifically tailored to these species. In Latin-American countries, *P. geniculatus* has been implicated in 50% of oral outbreaks, whereas other secondary vectors have been linked to outbreaks in Brazil, Venezuela, and Bolivia [6].

In the Casanare outbreak, we identified host mammals with identical DTUs as those found in patients (Table 1). Notably, in Casanare, *D. marsupials* has been directly implicated in a presumed large-scale oral outbreak [2]. Several outbreaks in Latin-American countries have involved other anthropogenic and wild mammals; this scenario of transmission could potentially be generated by dilution and/or effect caused by climatic change, habitat fragmentation, and urbanization [7,8]. For overall outbreaks, limitations were encountered in establishing the direct sources of oral transmission through parasite genotyping because we could only identify the DTU with PCR. A recent development, the amplicon-based nanopore sequencing approach for typing *T. cruzi*, has been successfully applied in an oral outbreak, offering precise detection of the source of oral transmission in the latest reported outbreak in Colombia [9,10].

In conclusion, Colombia has experienced a significant number of oral transmission outbreaks, emphasizing the need for continued surveillance and research [2,5,10,11]. An integrated approach combining scientific, epidemiologic, and logistical resources is essential for mitigating the occurrence of acute CD within the country.

Declarations of competing interest

The authors have no competing interests to declare.

Funding

This work was supported by Dirección de Investigación e Innovación from Universidad del Rosario.

Ethical review

The Colombian INS is designated as the reference laboratory in Colombia. INS is authorized under national law 9-1979, decrees 786-1990 and 2323- 2006, to use biospecimens and associated epidemiologic information without informed consent, including the anonymous disclosure of results. This study was performed following the Declaration of Helsinki and its later amendments, and all patient data were anonymized to minimize risk to participants.

Acknowledgments

The authors express their gratitude to the patients and the dedicated professionals at the Public Health laboratories in the affected departments for their invaluable efforts during these outbreaks. CH wants to dedicate this article to her niece EWH.

Author contributions

Conceptualization: APG, CH, JDR, MLSA. Methodology and data collection: APG, CH, CRA, MLSA, NB, LJC. Software, data curation: CH, CRA, MLSA. Analysis: CH, NL, CRA. Writing-original draft preparation: APG, CH, MLSA, LJC, CRA, MSA, MJV, RACD, SCA, ACF, LHP. Writing-reviewing and editing: CH, APM, JDR.

Data availability declaration

All the data of the manuscript are on the supplementary files.

Author agreement

All authors have seen and approved the final version of the manuscript being submitted. The article is the authors' original work, has not received prior publication, and is not under consideration for publication elsewhere.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijregi.2024.100410.

References

[1] De Sousa AS, Vermeij D, Ramos AN, Luquetti AO. Chagas disease. *Lancet* 2024;**403**:203–18. doi:10.1016/S0140-6736(23)01787-7.

[2] Hernández C, Vera MJ, Cucunubá Z, Flórez C, Cantillo O, Buitrago LS, et al. High-resolution molecular typing of Trypanosoma cruzi in 2 large outbreaks of acute Chagas disease in Colombia. *J Infect Dis* 2016;**214**:1252–5. doi:10.1093/infdis/jiw360.

[3] Hernández C, Cucunubá Z, Flórez C, Olivera M, Valencia C, Zambrano P, et al. Molecular diagnosis of Chagas disease in Colombia: parasitic loads and discrete typing units in patients from acute and chronic phases. *PLoS Negl Trop Dis* 2016;**10**:e0004997. doi:10.1371/journal.pntd.0004997.

[4] Rincón-Acevedo CY, Parada-García AS, Olivera MJ, Torres-Torres F, Zuleta-Dueñas LP, Hernández C, et al. Clinical and epidemiological characterization of acute Chagas disease in Casanare, Eastern Colombia, 2012–2020. *Front Med (Lausanne)* 2021;**8**:681635. doi:10.3389/fmed.2021.681635.

[5] Instituto Nacional De Salud *Boletín epidemiológico semanal 14 de 2023*. Bogota: Instituto Nacional De Salud; 2023.

[6] López-García A, Gilabert JA. Oral transmission of Chagas disease from a One Health approach: a systematic review. *Trop Med Int Health* 2023;**28**:689–98. doi:10.1111/tmi.13915.

[7] Ramírez JD, Montilla M, Cucunubá ZM, Floréz AC, Zambrano P, Guhl F. Molecular epidemiology of human oral Chagas disease outbreaks in Colombia. *PLoS Negl Trop Dis* 2013;**7**:e2041. doi:10.1371/journal.pntd.0002041.

[8] Vaz VC, D'Andrea PS, Jansen AM. Effects of habitat fragmentation on wild mammal infection by *Trypanosoma cruzi*. *Parasitology* 2007;**134**:1785–93. doi:10.1017/S003118200700323X.

[9] Cruz-Saavedra L, Ospina C, Patiño LH, Villar JC, Sáenz Pérez LD, Cantillo-Barraza O, et al. Enhancing trypanosomatid identification and genotyping with Oxford nanopore sequencing: Development and Validation of an 18S rRNA Amplicon-Based Method. *J Mol Diagn* 2024;**26**:323–36. doi:10.1016/j.jmoldx.2024.01.012.

[10] Gutiérrez SA, Jaimes-Dueñez J, Cruz-Saavedra L, Hernández C, Cantillo-Barraza O, Álvarez F, et al. An outbreak of acute Chagas disease possibly spread through oral transmission involving animal reservoirs in Eastern Colombia. *Am J Trop Med Hyg* 2024;**110**:36–9. doi:10.4269/ajtmh.23-0380.

[11] Vergara HD, Gómez CH, Faccini-Martínez ÁA, Herrera AC, López MJ, Camacho C, et al. Acute Chagas disease outbreak among military personnel, Colombia, 2021. *Emerg Infect Dis* 2023;**29**:1882–5. doi:10.3201/eid2909.230886.