Diagnosis of *Trypanosoma cruzi* infection among patients with non-ischemic cardiomyopathy presenting for clinical care in Houston, Texas

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Abstract word count: 49
Text word count: 878

Keywords: *Trypanosoma cruzi*, Chagas disease, Houston, Texas, cardiomyopathy, surveillance

Article Summary Line: We found a high prevalence of *T. cruzi* infection among Latino patients in a large, Houston cardiac clinic. Our results support a growing body of literature indicating that Chagas disease is not uncommon in the United States, and surveillance of Latino patients with nonischemic cardiomyopathy may be warranted.

Abstract

To better understand the epidemiology of *Trypanosoma cruzi* in Latino cardiac populations, we performed a cross-sectional study of 97 patients. A high prevalence of underdiagnosed infection and notable clinical diagnostic assay discrepancies were noted. Latino cardiac patients in the United States would benefit from laboratory screening for *T. cruzi* infection.

Chagas disease, caused by infection with *Trypanosoma cruzi* (*T. cruzi*) parasite, manifests as clinical disease in approximately one-third of patients, most often in cardiac form. Without treatment the parasite alternates between the trypomastigote and amastigote forms, resulting in direct smooth muscle tissue damage, myocardial fibrosis, chronic activation of inflammatory pathways, and autonomic dysfunction. This process will culminate years later as progressive heart failure for some patients. Chagas cardiomyopathy patients can present with malignant ventricular arrhythmias, aneurysms, thromboembolism, and/or sudden cardiac death. Despite advances in our understanding of the pathogenic pathways, it remains unknown why some patients will develop progressive cardiac disease while others will remain in a persistent subclinical indeterminate disease. Identification of infection status early, prior to development of heart failure is critical as chemotherapeutics are most efficacious in the acute and early stages of infection.

In the United States, an estimated 300,000 people are infected with *T. cruzi,* (1) and less than 1% have received treatment (2). Due to low physician awareness nationally (3), misdiagnosis or lack of Chagas disease diagnosis is likely common. Previous studies of patients from health programs in New York City and Los Angeles suggest that undiagnosed *T. cruzi* is particularly common among Latin American immigrants presenting with dilated cardiomyopathy (13-19%) (4, 5). However, the extent of U.S. *T. cruzi* infection beyond these two metropolitan areas is largely unknown. Our current study assessed the utility of *T. cruzi* diagnostic surveillance for Latino patients with nonischemic cardiomyopathy who presented for clinical care in a large tertiary-care facility in Houston, Texas.

From August 2015 to July 2017, we recruited cardiac patients for Chagas disease surveillance from Harris Health Ben Taub Hospital, a large county-funded tertiary care facility in

Houston, Texas. Patients with known nonischemic cardiomyopathy who presented to the outpatient cardiac clinic or who were admitted to a cardiac inpatient unit were invited to participate in our research study. Inclusion criteria required: (1) a recorded ejection fraction <50% within the past year and (2) a recent negative ischemic work-up based on stress echocardiography or invasive coronary angiography. We excluded patients of non-Latino ethnicity, who were currently incarcerated, had prior *T. cruzi* serology testing, evidence of acute coronary syndrome suspected to be of Takotsubo origin, or had documentation of an alternative etiology for their nonischemic cardiomyopathy (e.g., peripartum, genetic, alcoholic). Consent forms were available in English and Spanish and licensed translators ensured that all potentially eligible participants were invited to take part. This protocol was reviewed and approved by the Baylor College of Medicine Institutional Review Board (Protocol # H-36761).

Following consent, participating patients provided a blood sample for *T. cruzi* diagnostic testing and completed a risk factor questionnaire. The five page questionnaire was administered by a study team member, and included sections on 1) residential and travel histories, 2) potential triatomine exposures and sources, 3) current health symptoms, health behaviors and clinical family history, and 4) Chagas disease knowledge, attitudes, and practices. Initial *T. cruzi* diagnostic testing included *T. cruzi* specific antibody using Chagas STAT-PAK Assay (Chembio Diagnostic Systems, Inc., Medford, NY) and Hemagen Chagas Kit (Hemagen Diagnostics, Inc., Columbia, MD). Confirmation of positive and discordant results were then performed using Chagatest ELISA recombinante v3.0 (Wiener Laboratorios S.A.I.C., Rosario, Santa Fe, Argentina) and TESA blot by the U.S. Centers for Disease Control and Prevention (CDC) Parasitic Diseases Branch.

Over the two-year study period, 97 patients with nonischemic cardiomyopathy were enrolled out of 132 eligible patients; 35 refused to participate due to lack of interest. The average age of participants was 52 (range 28 to 91 years), and one-third were female. Birth countries for the cohort included Mexico (53%), USA (14%), El Salvador (12%), Honduras (9%), Guatemala (4%), and other Latin American Spanish-speaking countries (8%). USA born patients included Texas (n=9), New York (n=2), Indiana (n=1), and Oregon (n=1). Of the cohort, 43% reported having previously seen the triatomine vector. Of those who had seen the vector, 48% (20/42) reported sightings in Texas compared to 74% (31/42) in a Chagas-endemic Latin American country. Further, 12% of the cohort reported a history of triatomine bite(s). Despite high triatomine recognition, only 8% of the patient cohort had ever heard of Chagas disease and only half of these patients could correctly state how Chagas disease is acquired.

Overall, 7% of nonischemic cardiomyopathy Latino patients presenting for heart failure management were confirmed positive for *T. cruzi* infection by CDC confirmation testing. Discordant test results were common (Table 1), complicating the clinical decision-making process. All seven patients who had laboratory-confirmed Chagas cardiomyopathy were born in a Latin American country: El Salvador (n=4), Honduras (n=1), Mexico (n=1), and Venezuela (n=1). All seven confirmed positive patients had mothers born in and/or had lived in a Latin American country. Three had lived in a house with a dirt floor and two with a palm leaf thatched roof, which are known risks for triatomine infestations (6, 7). One had history of having received a blood transfusion in their home country. Two were polyparous mothers, and none of their children had been tested for Chagas disease. Only two of the seven patients with Chagas cardiomyopathy had previously heard of Chagas disease, and only one of these patients knew how Chagas disease was acquired.

Our study adds to the growing body of evidence supporting *T. cruzi* surveillance of Latino patients with non-ischemic cardiomyopathy or other risk factors for infection in the US. *T. cruzi* infection accounts for a considerable proportion of nonischemic cardiomyopathy in foreign-borne Latino patients (7-19% (4, 5)), and their timely diagnosis is imperative. Our investigation is not without limitations, which include the inability to perform additional cardiac imaging and diagnostic studies or follow patients long-term to evaluate prospective identification of underlying etiology. As highlighted by our discordant results, further work is needed to develop a highly specific diagnostic to prevent clinical confusion regarding accurate disease status. Determining the underlying etiology has benefit for Chagas cardiomyopathy patients even though treatment with antiparasitics (benznidazole and nifurtimox) has limited efficacy in these patients. Patients with Chagas cardiomyopathy may be recommended for heart transplant (8) and positively respond to implantable cardioverter-defibrillator placement (9) and amiodarone (10). Additionally, awareness of infection could lead to testing of at-risk family members who might respond favorably to early treatment.

Acknowledgements: We would like to thank Kaila Fagerstrom for assisting with patient recruitment. This project was funded by NIH NIAID R21 AI114877-01.

Disclaimer: The opinions expressed by authors contributing to this journal do not necessarily reflect the official position of the Centers for Disease Control and Prevention or the institutions with which the authors are affiliated.

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156 **Table 1: Discrepancies among four Chagas disease diagnostic assays***

ID	Age	Gender	Race	Ethnicity	State, Country of Birth	True Positive††	BCM Testing		CDC Confirmation Testing	
							Stat-Pak	Hemagen	Weiner EIA	Tesa Blot
CM-013	79	Female	Caucasian	Latino	Guerrero, Mexico	No	Faint Positive	(-)	(-)	NP
CM-014	66	Male	Caucasian	Latino	La Union, El Salvador	Yes	Positive	Positive	Positive	Positive
CM-017	62	Male	Caucasian	Latino	San Salvador, El Salvador	Yes	Positive	Positive	Positive	Positive
CM-037	73	Female	Caucasian	Latino	El Salvador †	Yes	Faint Positive	(-)	Positive	Positive
CM-048	54	Male	Caucasian	Latino	Texas, USA	No	Faint Positive	(-)	(-)	NP
CM-058	68	Female	Caucasian	Latino	Michoacan, Mexico	No	(-)	Positive	(-)	NP
CM-082	70	Female	Caucasian	Latino	Tegucigalpa, Honduras	Yes	Positive	Positive	Positive	Positive
CM-116	34	Male	Caucasian	Latino	Acapulco, Mexico	No	Faint Positive	(-)	(-)	NP
CM-121	77	Male	Caucasian	Latino	Maracay, Venezuela	Yes	Positive	Positive	Positive	Positive
CM-143	42	Male	Caucasian	Latino	San Miguel, El Salvador	Yes	Positive	Positive	Positive	Positive
CM-155	73	Male	Caucasian	Latino	(Unreported) †	No	Faint Positive	(-)	(-)	NP
CM-174	78	Male	Caucasian	Latino	Guerrero, Mexico	Yes	Positive	Positive	Positive	Positive
CM-197	62	Male	Caucasian	Latino	Tamaulipas, Mexico	No	Positive	(-)	(-)	NP
CM-243	54	Male	Caucasian	Latino	Durango, Mexico	No	Faint Positive	(-)	(-)	NP

NP=Not performed, (-)=Negative

*Eighty-three patients tested negative by Stat-Pak and Hemagen. This table displays the 14 patients who tested positive on at least one of the screener assays, whose samples where then sent to CDC for confirmation testing. None of the 83 patients who tested negative by the two screener assays were sent to CDC for confirmation testing.

†=Participants choose not to answer state and/or country of birth out of personal concerns

††= True Positive refers to the CDC guidelines recommending a minimum of two or more positive test results using two or more different diagnostic assay techniques: *https://www.cdc.gov/parasites/chagas/health_professionals/dx.html*

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