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Chagas Disease Infection among Migrants at the Mexico/Guatemala Border

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Abstract. Chagas disease results in the largest burden, in terms of disability-adjusted-life-years, of any parasitic disease in the Americas. Monitoring Chagas disease among migrants is critical to controlling its spread and to serving the needs of the migrant community. Therefore, we determined the prevalence and correlates of Chagas disease in regional and international migrant populations at the Mexico/Guatemala border. Data were collected as part of a larger study of human immunodeficiency virus (HIV) and migration. Participants were a sample of recent regional and international migrants who used an illicit substance or had recent problem drinking. *Trypanosoma cruzi* infection was classified as testing positive on two different enzyme-linked immunosorbent assays (ELISAs). Interviewer-administered surveys captured sociodemographics, migration history, Chagas disease knowledge, and access to care. We enrolled 389 recent migrants, and the prevalence of Chagas disease was 3.1%. Only 19% of the participants reported having ever heard of the disease and less than 1% had been previously tested. *Trypanosoma cruzi*–positive participants were more likely to have been born in a rural area or town than a city (92% yes versus 59% no, $P = 0.02$) and have recently lived in a house with a makeshift roof (33% yes versus 8% no, $P < 0.01$), walls (42% yes versus 13% no, $P < 0.01$), or floor (50% yes versus 21% no, $P < 0.02$), or cinderblock walls (92% yes versus 63% no, $P = 0.04$). With migration rapidly changing the distribution of Chagas disease, more work needs to be done to create targeted surveillance programs and provide access to affordable treatment among Latin American migrants.

INTRODUCTION

Human migration has led to the increasing urbanization and globalization of Chagas disease.[1–4] Latin American migrants may be particularly vulnerable to contracting Chagas disease both as a function of poverty premigration and living and working conditions during and post migration.[5,6] Although there is a growing body of literature describing Chagas disease in persons migrating from Latin America to Europe or the United States, there has been little study of internal migration within Latin America.[5,7,8]

Caused by the protozoan parasite *Trypanosoma cruzi*, Chagas disease has the largest burden of any parasitic disease in the Americas, with 7 million people currently infected.[9,10] Although the primary mode of transmission in rural areas is vector-borne, the disease can also be transmitted from mother to child, through blood donation, and less commonly, through tissue or organ transplantation.[11–13] Chagas disease has two main stages: an acute phase that lasts 6–8 weeks and a lifelong chronic phase. Among chronically infected individuals, 20–30% will go on to develop cardiac, gastrointestinal, or both cardiac and gastrointestinal damage.[13–15] Although current treatments are efficacious during the acute phase, challenges with drug side effects, and economic and logistical impediments to obtaining the drugs mean most people with the disease remain untreated.[13,16,17]

Traditionally, Chagas is considered a disease of rural poverty and low socioeconomic status—situations that are often the underlying push factors for migration.[18] In the rural areas, substandard housing conditions promote contact with vectors and are often used as a marker for determining risk. Although regional variations exist, mud floors, tile roof, and adobe walls have all been associated with either increased presence of the vector or infection.[19–22]

In addition, groups such as seasonal migrant farmworkers may have higher contact with vectors through their occupation.[6] For example, a 2009 qualitative study by Bayer et al.[6] in Peru suggested that the act of agricultural migrants circulating between temporary shelters in endemic regions and peri-urban communities puts them at risk for infection. Because Chagas disease is also transmitted in animals, they also suggested that the introduction of the rural practices of domestic animal husbandry into peri-urban areas with poor housing conditions may have facilitated the spread of the vector.[6,21,23,24]

Finally, because of stigma or discrimination against migrants and variable legal status, diminished access to health services may preclude diagnosis and treatment of Chagas disease.[6] In particular, undocumented migrants may be unwilling or unable to access health services. A recent systematic review found that current disease estimates among Latin American migrants are lacking, in part, because of scarce screening.[7]

Chagas disease is endemic in Mexico; however, current prevalence estimates are considered imprecise because official case reporting is not required.[25] A recent report by the World Health Organization (WHO) found Mexico had the highest number of annual cases because of congenital transmission and the second highest number of new cases because of vector transmission.[26] Prevalence estimates range from about 1% countrywide to as high as 13% in parts of the Mexican state of Chiapas at the Mexico–Guatemala border where vector transmission is high.[27,28] In Central America, Guatemala, El Salvador, and Honduras account for 85% of all new cases of Chagas disease.[26] In addition to higher disease burden, Guatemala, El Salvador and Honduras also have the greatest outmigration in Central America.[29] Given the confluence of increasing migration and the potential

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for a higher burden of disease among migrants, monitoring Chagas disease in this region is critical to controlling its spread and to serving the needs of the migrant community.

Determining the most at-risk individuals and creating targeted screening and surveillance programs are necessary for getting patients indicated for treatment into care, tracking the geographical spread of disease, and preventing nonvector disease transmission mechanisms. Therefore, the aims of this project were to: 1) determine the seroprevalence of Chagas disease in regional and international migrant populations at the Mexico/Guatemala border; 2) assess correlates of infection including migration history, sociodemographic, and socioeconomic variables.

MATERIALS AND METHODS

Study population and recruitment. Participants were recruited as part of a National Institute of Health (NIH)–funded cross-sectional study (*Cruzando Fronteras*) exploring substance use and human immunodeficiency virus (HIV) risk in migrants. From April to August 2015, 392 migrants were enrolled from sites along the Mexico/Guatemala border (175 in Mexico and 217 in Guatemala). Sample size requirements were based on the aims of the parent study, but were powered to capture low-prevalence outcomes (i.e., HIV). Recruitment sites were along major migration routes in and near the cities of Ciudad Hidalgo and Tapachula in Mexico and Quetzaltenango and Tecún Umán in Guatemala.

Participants were recruited using a combination of modified time-location sampling of migrant "venues" (e.g., migrant shelters) and peer referrals. To be enrolled in this study, participants must have been 1) at least 18 years of age; 2) able to speak Spanish; 3) willing and able to provide informed consent; 4) be willing to undergo testing for Chagas disease; 5) have used an illicit substance or have problem drinking in the past 2 months (criteria for the parent study, *Cruzando Fronteras*); and 6) meet the definition of a recent regional, international, or seasonal migrant. Recruiters used a brief screening questionnaire to assess eligibility for enrollment in the study.

Recent migrants included individuals with at least one of the following characteristics: 1) Moved states or countries within the past 5 years; 2) Traveled to another country or state for work for at least 3 months of the year or had a trip that lasted at least 1 month at a time; 3) Been deported within the past 5 years. All study activities were approved by The Human Research Protections Program of the University of California San Diego, the Comisión de Bioética del Estado de Chiapas, Mexico, and the Comité de Ética of the Universidad del Valle in Guatemala.

Laboratory methods. In Guatemala, serum samples were tested at a laboratory in Quetzaltenango using a commercially available recombinant ELISA, CHAGAS Rec, InVitro.†[30] The reported sensitivity is 97.4% and the specificity is 97.2%. In Mexico, serum samples were tested using an in-house ELISA at the Centro Regional de Investigación en Salud Pública and Instituto Nacional de Salud Pública (CRISP-INSP). All positive samples from Mexico were sent to the National Autonomous University of Mexico (UNAM) for their second ELISA test. Positive samples from Guatemala were given a second ELISA at CRISP.

The CRISP-INSP ELISA is based on Mexican strains of *T. cruzi* from Oaxaca as the source of the antigens, which has previously been shown to have good performance.[31,32] CRISP-INSP prepared antigens by culturing one of the strains characterized by UNAM and following the laboratory procedures developed by UNAM in collaboration with the Mexican National Blood Transfusion Center and Pan American Health Organization.[33] Positive and negative sera from UNAM serological bank were tested at CRISP-INSP and had a cut-off value of the optical density (OD) value of the negative sera plus two times the highest standard deviation value observed between the three replicates of OD values for positive sera. There is no published information on the specificity and sensitivity of the CRISP-INSP ELISA. The UNAM ELISA is based on strains of *T. cruzi* from Central Mexico and the sensitivity is reported as 96% and specificity as 100%.[34]

Per WHO guidelines for epidemiologic studies, *T. cruzi* infection may be considered for any sample that tests positive on two different ELISAs.[14] Therefore, we defined "positive" results as two positive ELISA results and "indeterminate" results for those who tested positive on only one ELISA.

Quantitative survey. As part of the *Cruzando Fronteras* project, eligible participants underwent a computer-assisted quantitative survey administered by local outreach workers trained in interviewing. Sociodemographic measures from the survey included in this analysis were age, gender, education level, civil status, rating of current financial situation, and indigenous ethnicity. We also specifically looked at whether the participant's main source of income came from agricultural work in the last year as this occupation was hypothesized to be associated with increased Chagas disease risk.

Migration variables examined included country and department (state) of birth, migration type (international, regional, or seasonal), whether they had migration documents, and whether they had ever been forced to move because of violence.

Participants were asked questions about the house they lived in the longest as a child and their most common housing situation in the past 6 months. Measures on housing included whether there were animals in or near the house, and if they saw triatomines in the house. Interviewers showed a photograph of triatomines and provided multiple local slang terms for the insect (e.g., *chinche*). Participants were also asked to report all construction materials that applied for the roof, walls, and floor of their childhood home and current living situation. Types of materials were grouped based on prior research and hypotheses about materials that may facilitate or hinder vector infestation.[19–22] Individuals were also asked if they were ever homeless in the past 6 months.

Chagas disease–specific questions included lifetime history of diagnosis or treatment of Chagas disease; history of blood transfusion; and whether they had a family member diagnosed with Chagas disease. Knowledge was assessed by

† The commercial test uses absorbance values at 450 nm (A_{450}) from weak positive, strong positive, and negative control sera to validate the test and the calculate cut-off value. The assay is considered valid only if the average A_{450} value of negative control is under 0.2, the weak positive A_{450} value is above 0.35 and strong positive gives is above 0.6. The cut-off value is the average A_{450} value of weak positive control divided by 1.5.

asking if they had ever heard of the disease and if it was possible to have Chagas disease and not know it.

We created a measure of Chagas disease transmission knowledge based on the following question: please tell me all the ways one can be infected with Chagas disease. Correct answer choices included triatomine, blood transfusion, mother to child, and organ transplant. Incorrect answer choices included mosquito, skin contact, and sexual contact. Correctly identified choices received a score of 1 and incorrect or "don't know" responses received a 0, for a total possible score of 7.

Statistical analysis. Descriptive statistics on demographics, migration history, childhood and recent housing characteristics, Chagas disease knowledge, and medical history were calculated for the total sample and by those who did and did not test positive for Chagas disease. Frequencies were calculated for dichotomous variables; age was nonnormal and continuous, and therefore, we calculated median and interquartile range (IQR). Pearson's χ^2 tests and Wilcoxon Rank Sum test were computed to compare variables with the outcome (Chagas disease). Using data from the screening survey, we also tested for differences between migrants and nonmigrants and between substance-using migrants and nonsubstance-using migrants. All analyses were run using SPSS software (SPSS Inc., Chicago, IL).

RESULTS

We tested 389 recent migrants for Chagas disease. Of these participants, 12 (3.1%) were positive for *T. cruzi*. The majority of migrants were born in Guatemala (49%), followed by Honduras (23%), El Salvador (18%), Mexico (6%), Nicaragua (3%), and Panama (< 1%) (Table 1). The median age of the sample was 31 and most were men (78%). Knowledge of Chagas disease was higher among those who tested positive for the disease (50% versus 18%, $P = 0.01$). Among those who had heard of Chagas disease, 71% knew it could be asymptomatic. The median score on the transmission knowledge questions was three (out of seven); 56% correctly identified triatomines as spreading the disease but only 12% knew about mother to child transmission. Only two (< 1%) people had been previously tested for Chagas disease. There were no statistically significant differences in demographic characteristics, migration history, or medical history between those tested positive for *T. cruzi* and those tested negative (Table 1). There was no difference between ever using illicit drugs (92% versus 76%, $P = 0.21$) or ever injecting illicit drugs (9% versus 11%, $P = 0.85$) among those who were Chagas positive versus negative.

Trypanosoma cruzi–positive participants were more likely to have been born in a ranch, farm, village, or town than in a city (92% versus 59%, $P = 0.02$) and more likely to have lived in a house with wooden walls (42% versus 17%, $P = 0.03$) (Table 2). There were no other statistically significant differences in housing characteristics at place of birth between the groups. In the past 6 months, *T. cruzi*–positive participants were more likely to have lived in a house with a makeshift roof (33% versus 8%, $P < 0.01$), walls (42% versus 13%, $P < 0.01$), or floor (50% versus 21%, $P < 0.02$). "Makeshift" materials included sleeping outdoors, or with nylon, plastic, or cardboard materials. They were also more likely to have lived in a home with cinderblock walls (92% versus 63%, $P = 0.04$).

DISCUSSION

Human migration represents both a risk for the reemergence of new Chagas disease infections and for the expansion of the geographical distribution of chronic Chagas cases. This is one of the first studies to look at the seroprevalence of Chagas disease infection among migrants in Central America and Mexico, which was found to be 3.1%. This is higher than the most current countrywide prevalence estimates, which range from 0.78 in Mexico to 1.2 in Guatemala.[26] Only two (< 1%) participants reported having ever previously been tested for Chagas disease, and knowledge of the disease was low. Early detection of Chagas disease is critical for both the patient and the larger community, especially given that treatment of Chagas disease is more efficacious when administered earlier in the disease progression.[13] In addition, a recent study found that blood donors seropositive for Chagas disease had 2.3 times higher risk of death by any cause as compared with seronegative donors.[35] Finally, asymptomatic infection remains a threat to public health because of the potential for mother to child and blood transmission.

We found differences in current housing materials between those with and without *T. cruzi* infection. Notably, those with *T. cruzi* infection lived in homes with extremely poor construction materials in the past 6 months (living outdoors or in tents) in a greater proportion than those without the infection. Past studies have shown associations between housing materials and greater triatomine infestation.[19–22] Although we found that recent living in housing with makeshift materials was associated with Chagas disease, this may be a proxy for disadvantaged socioeconomic status rather than an indicator of recent infection. However, because we are unable to determine when or how a person became infected with Chagas disease, we cannot formally test that hypothesis. Either outcome points to the fact that Chagas is a disease of poverty and that poverty may persist even after moving out of rural areas. Thus any Chagas disease testing campaigns in rural and urban areas should target people living in substandard housing.

Whereas current housing materials differed between those with and without *T. cruzi* infection, we only found that living in a childhood home with wooden walls was associated with infection. Past studies have found mixed associations of particular housing materials based on both the region and the species of the vector.[19–22] Because our sample of migrants came from multiple countries and regions, it may have masked any ability to detect significant effects. In addition, the longer period of recall for participants may have resulted in inaccurate reporting of housing materials during childhood. However, any recall bias would likely be equal among those with and without Chagas disease as no participants knew of their disease status at the time of the interview.

Similar to other studies, we found more *T. cruzi*–positive individuals were born in rural areas than in cities compared with participants negative for *T. cruzi*.[36–38] Although there is growing evidence that domiciliated vectors have spread to urban and peri-urban areas, most of the current infections still arise in rural regions.[39–41] Participants were born in geographically disparate departments ("states") with varying levels of poverty. This points to the utility of screening programs that cast a wider net in addition to targeting of highly endemic areas. Recent economic evaluations of the cost of Chagas disease have found that not screening for chronic

TABLE 1
Characteristics of migrants with and without Chagas disease (N = 389)

Variable	Total (N = 389) N (%)	*Trypanosoma cruzi* Negative (N = 377) N (%)	*Trypanosoma cruzi* Positive (N = 12) N (%)	P value§
Country of interview				
Guatemala	214 (55)	205 (54)	9 (75)	0.16
Mexico	175 (45)	172 (46)	3 (25)	
Demographics and behaviors				
Median age (IQR)	31 (24–37)	31 (24–37)	33 (24–43)	0.68
Biological sex	–	–	–	0.66
Female	85 (22)	83 (82)	2 (17)	
Male	304 (78)	294 (78)	10 (83)	
Less than secondary education (ref: secondary or above)	227 (58)	219 (58)	8 (67)	0.55
Married/common law (ref: single, divorced, separated, widow)	277 (71)	268 (71)	9 (75)	0.78
Current financial situation bad to extremely bad (ref: extremely good to neutral)	204 (52)	195 (52)	9 (75)	0.11
Member of indigenous group	38 (9)	37 (10)	1 (8)	0.84
Agricultural worker, past year	36 (9)	34 (9)	2 (17)	0.39
Since birth, rural area for more than 6 mo?	235 (60)	228 (61)	7 (58)	0.88
Migration				
Country of Birth				
Mexico	23 (6)	23 (6)	0 (0)	0.38
Guatemala	192 (49)	187 (50)	5 (42)	0.59
Honduras	91 (23)	88 (23)	3 (25)	0.89
El Salvador	71 (18)	67 (18)	4 (33)	0.17
Nicaragua	11 (3)	11 (3)	0 (0)	0.55
Panama	1 (< 1)	1 (< 1)	0 (0)	–
International migrant, past 5 years	261 (67)	252 (67)	9 (75)	0.58
Regional migrant, past 5 years	213 (55)	205 (55)	8 (67)	0.42
Seasonal migrant, past year	235 (60)	226 (62)	9 (75)	0.36
Current undocumented migrant	198 (51)	193 (51)	5 (42)	0.52
Knowledge				
Have you ever heard of Chagas disease?	**75 (19)**	**69 (18)**	**6 (50)**	**0.01**
Transmission knowledge score (out of 7) (IQR) (N = 75)	3 (2–4)	3 (2–4)	3 (2–4)	0.98
Is it possible to have Chagas disease and not know it? (N = 75)	53 (71)	50 (73)	3 (50)	0.35
Medical				
Have you ever been tested for Chagas disease?	2 (< 1)	1 (< 1)	1 (8)	0.06
Have you ever been told by a healthcare provider you have Chagas disease?	0 (0)	0 (0)	0 (0)	–
Has anyone in your family been told by a healthcare provider they have Chagas disease?	3 (1)	3 (1)	0 (0)	1.00
Have you ever received a blood transfusion?	54 (14)	54 (14)	0 (0)	0.16

Items in bold are significant at $P < 0.05$.
§ P-values are based on chi-square tests, non-parametric Wilcoxon rank sum tests or Fisher's Exact test.

cases is most costly to healthcare systems.[42,43] However, the benefits of screening are diminished if improvements in diagnostic testing and availability of efficacious treatment are not made in tandem.

Knowledge of Chagas disease in our sample was low, with only 19% of participants reporting having ever heard of the disease. However, knowledge of the disease was higher among those who had the disease (50%), suggesting they may have been exposed to educational campaigns in their country of origin. This could be because of more extensive educational campaigns in rural areas of Central America. Among those who had heard of the disease, 44% did not recognize triatomines as transmitting the disease and 88% did not know it was spread from mother to child. Therefore there is a need for increased educational campaigns among all individuals staying in areas such as this border region.

The median age of individuals tested positive for *T. cruzi* was 33 (IQR: 24–43). The potential progression from asymptomatic (indeterminate) to the symptomatic determinate form usually occurs 10–30 years after the initial infection. Given that the spraying campaigns for Chagas disease were started in the 1990s, it is expected the cohort of individuals infected before the campaigns are still coming into the age of reactivation.[13] However this study did not assess symptoms of participants and, thus, we are unable to classify participants as having indeterminate or determinate infection.

Limitations. The data presented here are from a nonrandom sample of substance-using migrants, and therefore, may not be

TABLE 2
Characteristics of housing and housing materials of recent migrants by Chagas disease status

	Trypanosoma cruzi Negative (*N* = 377) N (%)	*Trypanosoma cruzi* Positive (*N* = 12) N (%)	*P* value§
Childhood home			
Type of place of birth (ranch/farm/ village/town vs. city)	**222 (59)**	**11 (92)**	**0.02**
Seen triatomine in house?	184 (50)	6 (50)	0.97
Animals in/near home?	321 (85)	9 (75)	0.34
Roof (select all)			
Thatched (straw, palm)	32 (9)	0 (0)	0.29
Wood	7 (2)	0 (0)	0.63
Cement	40 (11)	0 (0)	0.23
Metal (tin, iron, steel)	229 (61)	8 (67)	0.68
Tile (clay, shingles)	76 (20)	4 (33)	0.27
Makeshift (none, nylon, plastic, cardboard)	1 (< 1)	0 (0)	1.00
Walls (select all)			
Natural (bamboo, adobe, dirt, palm)	124 (33)	4 (33)	0.97
Wood	**64 (17)**	**5 (42)**	**0.03**
Makeshift (none, nylon, plastic)	8 (2)	0 (0)	0.61
Cinderblock	141 (37)	3 (25)	0.38
Metal (aluminum)	8 (2)	0 (0)	0.61
Durable (cement, brick, drywall, rock)	71 (19)	1 (8)	0.36
Floor (select all)			
Wood	5 (1)	0 (0)	1.00
Durable (cement, brick, granite, rock)	167 (44)	4 (33)	0.45
Metal (iron)	–	–	
Tile	67 (18)	1 (8)	0.40
Makeshift (dirt, outdoors, cardboard)	152 (40)	8 (67)	0.07
Recent housing, past 6 months			
Seen triatomine in places slept/stayed?	79 (21)	3 (25)	0.74
Animals in/near places slept/stayed?	227 (60)	9 (75)	0.30
Ever homeless, past 6 months	145 (39)	4 (33)	0.72
Roof (select all)			
Thatched (straw, palm)	27 (7)	2 (17)	0.22
Wood	29 (8)	1 (8)	0.94
Cement	137 (37)	4 (33)	0.82
Metal (tin, iron, steel)	247 (66)	9 (75)	0.51
Tile (clay, shingles)	32 (9)	1 (8)	0.98
Makeshift (none, nylon, plastic, cardboard)	**31 (8)**	**4 (33)**	**< 0.01**
Walls (select all)			
Natural (bamboo, adobe, dirt, palm)	58 (16)	1 (8)	0.50
Wood	39 (10)	2 (17)	0.49
Makeshift (none, nylon, plastic)	**48 (13)**	**4 (42)**	**< 0.01**
Cinderblock	**237 (63)**	**11 (92)**	**0.04**
Metal (aluminum)	4 (1)	0 (0)	1.00
Durable (cement, brick, drywall, rock)	133 (36)	2 (17)	0.18
Floor (select all)			
Wood	11 (3)	0 (0)	0.55
Durable (cement, brick, granite, rock)	267 (71)	9 (75)	0.76
Metal (iron)	2 (1)	0 (0)	1.00
Tile	116 (31)	3 (25)	0.67
Makeshift (dirt, outdoors, cardboard)	**80 (21)**	**6 (50)**	**0.02**

Items in bold are significant at $P < 0.05$.
§ *P*-values are based on chi-square tests, non-parametric Wilcoxon rank sum tests or Fisher's Exact test.

generalizable to all migrants in the region. However, using data from screening visits, we found no difference between substance users and nonsubstance users in terms of Chagas disease knowledge, prior Chagas disease testing, or living in a rural area (data not shown). Also, as most people become infected with *T. cruzi* as a child, we would not expect different prevalence estimates of disease between the two groups.[15]

No screening gold standard test exists for Chagas disease; however, the use of two different ELISAs, in particular the use of locally developed tests, strengthens our findings. Although there may be some misclassification due to poor screening tests, the direction of our findings were in line with both past literature and hypothesized outcomes. Data were cross–sectional, so we could not determine when a particular individual was infected with Chagas disease. However, we believe the findings still provide a useful snapshot of prevalence in this southern Mexico/Guatemala border region. Finally, our sample was predominantly men, and given the risk of mother to child transmission, future studies should focus on screening for Chagas disease among migrant women.

CONCLUSIONS

With migration rapidly changing the distribution of Chagas disease, there is a need to identify those who are chronically infected. Spain, the United States, and other nonendemic countries are increasingly recognizing the importance of screening for Chagas disease within migrant communities.[5,44,45] Because of the potential for advanced cardiac disease and congenital transmission in persons with undiagnosed and untreated chronic Chagas disease, more work needs to be done to create targeted surveillance programs and provide access to affordable treatment.

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