Prevalence of Chagas Heart Disease in a Region Endemic for *Trypanosoma Cruzi*
Evidence From a Central Bolivian Community

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ABSTRACT

Background: Though the incidence of new *Trypanosoma cruzi* infections has decreased significantly in endemic regions in the Americas, medical professionals continue to encounter a high burden of resulting Chagas disease among infected adults. The current prevalence of Chagas heart disease in a community setting is not known; nor is it known how recent insecticide vector control measures may have impacted the progression of cardiac disease in an infected population.

Objectives: We sought to determine the current prevalence of *T. cruzi* infection and associated Chagas heart disease in a Bolivian community endemic for *T. cruzi*.

Methods: Nested within a community serosurvey in rural and periurban communities in central Bolivia, we performed a cross-sectional cardiac substudy to evaluate adults for historical, clinical, and electrocardiographic evidence of cardiac disease. All adults between the ages of 20 and 60 years old with *T. cruzi* infection and those with a clinical history, physical exam, or electrocardiogram consistent with cardiac abnormalities were also scheduled for echocardiography.

Results: Of the 604 cardiac substudy participants with definitive serology results, 183 were seropositive for infection with *T. cruzi* (30.3%). Participants who were seropositive for *T. cruzi* infection were more likely to have conduction system defects (1.6% vs. 0% for complete right bundle branch block and 10.4% vs. 1.9% for any bundle branch block; p = 0.008 and p < 0.001, respectively). However, there was no statistically significant difference in the prevalence of bradycardia among seropositive versus seronegative participants. Echocardiogram findings were not consistent with a high burden of Chagas cardiomyopathy: valvulopathies were the most common abnormality, and few participants were found to have low ejection fraction or left ventricular dilatation. No participants had significant heart failure.

Conclusions: Though almost one-third of adults in the community were seropositive for *T. cruzi* infection, few had evidence of Chagas heart disease.
community-wide prevalence of *T. cruzi* infection, and a nested study of cardiac disease in adults 20 to 60 years old.

**METHODS**

**Ethics statement**

The protocol was approved by the institutional review boards of CEADES, Asociación Benéfica PRISMA, and Johns Hopkins Bloomberg School of Public Health. All adult participants provided written informed consent, with separate forms for the serosurvey and the cardiac substudy. Written informed consent was obtained from the parent or guardian on behalf of children younger than 18 years old, and children aged 7 to 17 years provided written assent.

**Study setting and serosurvey participants**

The study was conducted in Punata, a province of Cochabamba Department with a population of 47,735 inhabitants at the time of the 2001 census. Participants were recruited between January 2009 and May 2010. Communities were selected to include rural and periurban populations living in the catchment area of Punata Hospital, located in the central city (also called Punata). Field-workers invited all residents 2 years or older to participate. All participating individuals provided a blood sample for serologic testing. Testing was also offered for children younger than 2 years whose mothers were found to have *T. cruzi* infection, based on the risk of congenital transmission.

**Adult cardiac substudy**

All permanent community residents in the age range of 20 to 60 years who participated in the serosurvey were asked to participate in the nested cardiac substudy. Adults older than 60 years were excluded based on previous evidence that rates of Chagas heart disease peaked in adults ages 30 to 60 years old [9–12]. They were also excluded to reduce the number of age-related nonspecific cardiac findings on electrocardiograms (ECG) and echocardiograms.

**Laboratory methods**

Serum samples were evaluated for antibodies to *T. cruzi* using at least 2 of 3 commercially available assays: a rapid immunochromatographic screening test based on recombinant *T. cruzi* antigens (STAT-PAK, Chembio Diagnostic Systems, Inc., Medford, New York); an epimastigote lysate enzyme-linked immunosorbent assay (Chagatik, bio-Mérieux, Buenos Aires, Argentina); and an indirect hemagglutination assay (IHA—Chagatest, Wiener Laboratorios, Rosario, Argentina). All tests were performed and interpreted following the manufacturers’ guidelines. Individuals were considered to have *T. cruzi* infection if they had 2 positive serologic tests. Twelve individuals participating in the nested cardiac substudy had inconclusive serologic results based on conflicting or indeterminate assay results; these individuals were excluded from analysis.

**Cardiac study procedures**

All substudy participants underwent a focused history and physical exam and an ECG and gave 1 blood sample. All individuals who were positive for infection with *T. cruzi* and all those with any evidence of cardiac abnormalities by history, physical exam, or ECG (including bradycardia with a heart rate <60 beats/min) were scheduled to undergo echocardiogram. Echocardiograms were performed using a portable Esaote Caris machine (Genoa, Italy). A cardiologist read all ECG and performed and interpreted all echocardiograms. ECG were coded and interpreted according to established criteria [13]. The cardiologist was blinded for all ECG interpretations; study participants occasionally revealed their *T. cruzi* infection status to the cardiologist during their echocardiogram rendering echocardiogram blinding incomplete.

**Statistical analysis**

We evaluated associations between infection with *T. cruzi* and cardiac lesions using odds ratios with 95% confidence intervals (CI) and 2-tailed Fisher exact test with an alpha of 0.05, as well as multivariate logistic regression models. Logistic regression models included age and serostatus as predictor covariates. Because incomplete right bundle branch block (RBBB) has been shown to be a highly nonspecific finding and can be a normal variant in healthy adults [14], all analyses evaluating combined conduction system defects excluded incomplete right bundle branch blocks. Data were collected and managed using Microsoft Access (Redmond, WA, USA); statistical analysis was performed using Stata (version 11.0, IBM, Armonk, NY, USA).

**RESULTS**

**Study population**

A total of 1,380 individuals participated in the *T. cruzi* serosurvey; 36 individuals (2.6%) were excluded due to inconclusive serology results, yielding a survey population of 1,344 (Table 1). The mean age of all participants in the community serosurvey was 31.29 ± 21.83 years. The mean age of the participants in the cardiac substudy was 39.19 ± 12.16 years, and among those who received an echocardiogram was 39.89 ± 12.26 years. Seroprevalence increased with increasing age in all decades until the seventh decade, with a maximum seroprevalence of 56.88% among study participants between the ages of 60 and 69 years. Rates were lower among study participants in their 70s and 80s but with confidence intervals that overlapped with those in younger age groups. Twenty-one of 52 participants between the ages of 70 and 79 years were positive for *T. cruzi* infection, yielding a seroprevalence of 40.38% (95% CI: 27.31 to 54.87). Of those participants between the ages of 80 and 89 years, 7 of 18 were positive for *T. cruzi* infection, yielding a seroprevalence of 38.89% (95% CI: 18.26 to 63.86) (Figure 1).
Cardiac disease according to *T. cruzi* infection

Of 632 eligible adults, 604 (95.6%) participated in the cardiac study; 183 (30.3%) had confirmed *T. cruzi* infection. Three seropositive participants (1.6%) had complete RBBB on ECG (1.6%) compared with none of the seronegative participants (*p* = 0.008) (Table 2). Nineteen *T. cruzi*-infected participants had any conduction system defect, compared with 8 seronegative participants (10.4% vs. 1.9%, *p* < 0.001). The percentages with bradycardia were similar among those with and without *T. cruzi* infection (3.8% vs. 4.7%, respectively, for heart rate <50 beats/min).

The prevalence of RBBB was highest in seropositive individuals older than 40 years, whereas bifasicular blocks were read more commonly in younger seropositive participants (Figure 2). The prevalence of any conduction system defect among both seropositive and seronegative individuals was highest among those between the ages of 20 and 29 years: 23.1% and 2.6% among seropositive and seronegative individuals, respectively. In multivariable logistic regression models adjusted for sex and age (by decade), bifasicular block and any conduction system defect were significantly associated with *T. cruzi* infection (odds ratio for bifasicular block 8.19, 95% CI: 1.55 to 43.17, *p* < 0.001) and any conduction system defect 7.36, 95% CI: 2.97 to 18.6, *p* < 0.001).

DISCUSSION

Our study was one of the first in decades to evaluate the community burden of *T. cruzi* infection and Chagas heart disease in the inter-Andean valleys of Bolivia. Housing improvement programs began in Cochabamba in the 1990s, and household insecticide application was instituted on a large scale by the Bolivian National Chagas Disease Control Program between 2000 and 2004 (personal communication, F. Torrico, 2009) [15]. Our data support the success of these efforts. We found a much lower prevalence of *T. cruzi* infection than a study conducted in Cochabamba Department in 1988 did (74% in 1988 vs. 23% in our data) and a strikingly lower prevalence in children (38% in 1988 vs. 5.6% in our data) [12]. Although our age range and case definitions varied from those used in the 1988 study, it is interesting to note
that we also found a lower rate of bundle branch blocks among infected participants than the 1988 study did (20% in 1988 vs. 10.4% in our data), and we found no participants with clinically evident congestive heart failure (compared with 9% in the 1988 data) [12]. A similar study restricted to Bolivian women of childbearing age in the 1980s also showed higher rates of conduction system abnormalities than we found [11]. Nevertheless, T. cruzi infection is still a significant risk factor for conduction system defects in our data. These findings provide an optimistic picture for the future, because bundle branch blocks [10], decreased ejection fraction [16,17], left and right ventricular dysfunction [18,19], and abnormal diastolic function [20,21] have all been associated with increased mortality in individuals with Chagas disease. Evidence from mouse models [22,23] and communities [24] suggest that continued vector-borne exposure to T. cruzi may increase the risk of Chagas cardiomyopathy. Failure to down-regulate the anti-T. cruzi inflammatory immune response is widely accepted as an important driver of Chagas cardiomyopathy development and progression [25,26]. Vector-borne parasite exposure is hypothesized to maintain sustained antigen exposure and consequent higher chronic inflammatory immune responses, contributing to Chagas cardiomyopathy. The lower rate of clinical disease in our study may reflect the better vector control over the previous decades and decreased exposure to the

### TABLE 2. ECG findings* in individuals with and without T. cruzi infection

<table>
<thead>
<tr>
<th>Heart rate rhythm</th>
<th>Seropositive (n = 183)</th>
<th>Seronegative (n = 421)</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate &lt; 60 beats/min</td>
<td>63 (34.4)</td>
<td>128 (30.4)</td>
<td>1.202</td>
<td>0.815–1.764</td>
<td>0.329</td>
</tr>
<tr>
<td>Heart rate &lt; 50 beats/min</td>
<td>7 (3.8)</td>
<td>20 (4.8)</td>
<td>0.797</td>
<td>0.280–2.009</td>
<td>0.613</td>
</tr>
<tr>
<td>Mean heart rate</td>
<td>62.65 ± 9.4</td>
<td>62.66 ± 10.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation/flutter</td>
<td>0</td>
<td>1 (0.2)</td>
<td>0.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventricular arrhythmia (PVC)</td>
<td>1 (0.5)</td>
<td>0</td>
<td>0.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Bundle branch blocks</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RBBB (complete)</td>
<td>3 (1.6)</td>
<td>0</td>
<td>0.0</td>
<td></td>
<td>0.027</td>
</tr>
<tr>
<td>LAFB</td>
<td>7 (3.8)</td>
<td>5 (1.2)</td>
<td>3.309</td>
<td>0.888–13.378</td>
<td>0.052</td>
</tr>
<tr>
<td>LPFB</td>
<td>3 (1.6)</td>
<td>1 (0.2)</td>
<td>7.000</td>
<td>0.556–36.280</td>
<td>0.085</td>
</tr>
<tr>
<td>Bifascicular block</td>
<td>6 (3.3)</td>
<td>2 (0.5)</td>
<td>7.102</td>
<td>1.250–72.337</td>
<td>0.006</td>
</tr>
<tr>
<td>Any BBB†</td>
<td>19 (10.4)</td>
<td>8 (1.9)</td>
<td>5.981</td>
<td>2.432–16.061</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Incomplete RBBB</td>
<td>13 (7.1)</td>
<td>29 (6.9)</td>
<td>1.034</td>
<td>0.481–2.112</td>
<td>0.924</td>
</tr>
<tr>
<td><strong>Other abnormalities</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1° AV block</td>
<td>4 (2.2)</td>
<td>4 (1.0)</td>
<td>2.330</td>
<td>0.428–12.633</td>
<td>0.253</td>
</tr>
<tr>
<td>ST-T changes</td>
<td>13 (7.1)</td>
<td>13 (3.09)</td>
<td>2.400</td>
<td>1.001–5.739</td>
<td>0.025</td>
</tr>
<tr>
<td>Low voltage QRS</td>
<td>0</td>
<td>1 (0.2)</td>
<td>0.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal ECG</td>
<td>88 (48.1)</td>
<td>228 (54.2)</td>
<td>0.171</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are n (%) or mean ± SD, unless otherwise indicated.
AV, atrioventricular; BBB, bundle branch block; ECG, electrocardiogram; LAFB, left anterior fascicular block; LPFB: left posterior fascicular block; LVH, left ventricular hypertrophy; PVC, premature ventricular contraction; RBBB: right bundle branch block; T. cruzi, Trypanosoma cruzi.

*No participant was found to have LVH or an abnormal initial portion of their QRS complex on ECG.
†By 2-tailed Fisher exact test.
‡Any complete bundle branch block (RBBB, LAFB, LPFB, bifascicular block).

FIGURE 2. Electrocardiogram findings by age and Trypanosoma cruzi serostatus. AV, atrioventricular.
parasite. However, further data are needed to better understand this possible association.

Our observation of an association between T. cruzi infection and left atrial dilation is intriguing but its clinical significance is unclear. Previous studies have found left atrial dilation associated with RBBB in infected individuals, perhaps indicating early manifestations of cardiac involvement [27–29]. Furthermore, left atrial dilation has been linked to increased risk of sudden cardiac death in those with known Chagas cardiomyopathy [20,21]. The most common abnormalities found on echocardiogram were valvulopathies, most commonly isolated aortic sclerosis in participants between 50 and 60 years old. This finding was consistent with previous studies and is most consistent with age-related changes [30]. We anticipated seeing a greater burden of valvular disease associated with known or suspected rheumatic heart disease, which most commonly causes mitral stenosis; it is not common to have aortic disease resulting from rheumatic heart disease without concomitant mitral involvement [31,32]. We found no association between valvulopathies and T. cruzi infection.

**Study limitations**

First, it is possible that those individuals who were in poor health did not present to our mobile clinic to participate in the study, and we therefore underestimated the cardiac disease burden. Second, we excluded adults over age 60 years to minimize nonspecific cardiac disease such as paroxysmal atrial fibrillation. Although the work of Lima-Costa et al. [33,34] indicates that Chagas may be a greater problem in elderly patients than was previously recognized, previous studies have found the majority of cardiac disease developing in adults between 30 and 50 years old [9–12]. It is possible, however, that our exclusion of adults over age 60 reduced the amount of Chagas heart disease detected. Finally, our echocardiogram findings may have been affected by the low rates of echocardiogram completion. However, consensus among Chagas experts indicates that the rate of

**TABLE 3.** Comparing those who did and did not complete echocardiograms, by serostatus, in those who were scheduled for study per protocol

<table>
<thead>
<tr>
<th></th>
<th>Chagas Seropositive</th>
<th>Chagas Seronegative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Received Echo (n = 78)</td>
<td>No Echo (n = 105)</td>
</tr>
<tr>
<td>Mean age, yrs</td>
<td>44.0 ± 11.2</td>
<td>43.4 ± 11.6</td>
</tr>
<tr>
<td>Female</td>
<td>46 (59.0)</td>
<td>61 (58.1)</td>
</tr>
<tr>
<td>Heart rate &lt;60 beats/min</td>
<td>28 (35.9)</td>
<td>35 (33.3)</td>
</tr>
<tr>
<td>Heart rate &lt;50 beats/min</td>
<td>4 (5.1)</td>
<td>3 (2.9)</td>
</tr>
<tr>
<td>Bifascicular block</td>
<td>3 (3.9)</td>
<td>3 (2.9)</td>
</tr>
<tr>
<td>Any conduction system defect</td>
<td>6 (7.7)</td>
<td>13 (12.4)</td>
</tr>
</tbody>
</table>

Values are mean ± SD or n (%).

**TABLE 4.** Echocardiography findings* in individuals with and without T. cruzi infection

<table>
<thead>
<tr>
<th></th>
<th>Seropositive (n = 78)</th>
<th>Seronegative (n = 122)</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV end-diastolic diameter</td>
<td>4.58 ± 0.94</td>
<td>4.42 ± 0.79</td>
<td>0.207</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEF</td>
<td>0.68 ± 0.16</td>
<td>0.68 ± 0.12</td>
<td>0.959</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LA diameter</td>
<td>3.00 ± 0.84</td>
<td>2.84 ± 0.68</td>
<td>0.149</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV dilation</td>
<td>4 (5.1)</td>
<td>3 (2.4)</td>
<td>2.144</td>
<td>0.351–14.989</td>
<td>0.435†</td>
</tr>
<tr>
<td>LAD</td>
<td>7 (9.0)</td>
<td>2 (1.6)</td>
<td>5.915</td>
<td>1.077–59.355</td>
<td>0.030†</td>
</tr>
<tr>
<td>EF &lt;55%</td>
<td>2 (2.6)</td>
<td>3 (2.5)</td>
<td>1.044</td>
<td>0.853–9.329</td>
<td>1.000†</td>
</tr>
<tr>
<td>Any valvulopathy</td>
<td>8 (10.3)</td>
<td>8 (6.5)</td>
<td>1.629</td>
<td>0.506–5.215</td>
<td>—</td>
</tr>
<tr>
<td>Early systolic dysfunction</td>
<td>2 (2.6)</td>
<td>1 (0.8)</td>
<td>3.184</td>
<td>0.162–189.36</td>
<td>0.562†</td>
</tr>
<tr>
<td>LVH</td>
<td>62 (79.5)</td>
<td>96 (78.7)</td>
<td>1.049</td>
<td>0.495–2.274</td>
<td>0.892†</td>
</tr>
</tbody>
</table>

Values are mean ± SD or n (%), unless otherwise indicated.

EF, ejection fraction; LA, left atrium; LAD, left atrial dilation; LV, left ventricle; LVEF, left ventricular ejection fraction; LVH, left ventricular hypertrophy.

*No participant was found to have an apical aneurysm, an intracavitary thrombus, or diffuse wall motion abnormalities on echocardiogram.

†By 2-tailed Fisher exact test.
clinically significant Chagas heart disease is rare in the absence of ECG abnormalities [35].

CONCLUSIONS
Our study found low rates of Chagas cardiomyopathy in a community endemic for T. cruzi, possibly related to the effects of widespread vector control efforts over the previous 20 years. More research is needed to better understand who, among those infected with T. cruzi, is at increased risk of progression to associated disease.

ACKNOWLEDGMENTS
The authors would like to thank Drs. Rene Ugarte, Marco Solano Mercado, and Gimena Rojas Delgadillo for their assistance in the laboratory and in the field. They would additionally like to thank all the members of the field team who collected data and specimens for the community study, and the members of CEADES Salud y Medio Ambiente who assisted with data collection and management.

REFERENCES