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Original papers

Low seroprevalence of *Trypanosoma cruzi* infection and chronic chagasic cardiomyopathy in a region with abundance of triatomine vectors in Yucatan Peninsula of Mexico[1]

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ABSTRACT. The Yucatan Peninsula of Mexico is endemic with Chagas disease. The main vector responsible for *Trypanosoma cruzi* transmission is *Triatoma dimidiata* which is abundant in domestic, peridomestic and sylvan cycles. The abundance of vectors favours *T. cruzi* transmission and is a high risk for developing chronic chagasic cardiomyopathy (CCC). In the past 10 years, little information was available on parasite seroprevalence and the prevalence of CCC in the Yucatan Peninsula. In the present work, we studied two Mayan communities with a high abundance of *T. dimidiata* and a random serial sample of 233 patients with an altered electrocardiogram or cardiac failure admitted to the Regional Hospital. A homemade enzyme-linked immunosorbent assay and indirect immunofluorescence standardized techniques were used to detect anti-*T. cruzi* IgG. In addition, Mayan volunteers were monitored by electrocardiography. In the Mayan communities, 4.8% (3/63) subjects were positive for *T. cruzi* antibodies none of them presented electrocardiographic alterations, however in seronegative subjects were detected right or left ventricle hypertrophy in 25% (16/63). A remarkable finding was that 90% of the Mayan population recognized the vector and 65% of them had experienced contact with triatomines bites. At the Regional Hospital 0.42% (1/233) were positive for *T. cruzi* antibodies showing compatible diagnosis with CCC; the most frequent pathology in this population was hypertension in 65% (151/233) and the less frequent was dilated myocardiopathy 6% (14/233). In conclusion, the prevalence of *T. cruzi* infection and CCC can be considered low in Yucatan, Mexico.

Key words: *Trypanosoma cruzi*, Chagas disease, seroprevalence, IgG, chronic chagasic cardiomyopathy

Introduction

The Yucatan Peninsula of Mexico is endemic with Chagas disease. The main vector responsible for *Trypanosoma cruzi* transmission is *Triatoma dimidiata* which is abundant in domestic, peridomestic, and sylvan cycles [1–3]. The abundance of vectors favours *T. cruzi* transmission and is a high risk for developing chronic chagasic cardiomyopathy (CCC). In the past 10 years, little information was available on seroprevalence and the prevalence of CCC in Yucatan. In blood banks, seroprevalence has been estimated between 0.5% and 0.7% [4–5]. Surveys have indicated seroprevalence rates of 0.1% in urban [6] and 2.3% in rural communities [7–8]. However, prevalence of CCC in Regional Hospitals has been poorly studied. In 2011, it was reported that 15% (13/91) of patients diagnosed with dilated myocardiopathy corresponded to CCC [9].

Chagas disease is considered the most important parasitic disease in Mexico [10] with 1.5 to 2 million Mexicans infected with *T. cruzi*; this estimation is based on the finding that 1.5% of blood donations are contaminated [11]. In addition to 31 autochthonous species of Triatominae found in

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Mexico spread over the country are infected [12].

In the present work, we search for *T. cruzi* infection in two Mayan communities with a high risk of infection. We also searched for cases of CCC at the Regional Hospitals attending the area.

Material and Methods

The study was conducted in two Mayan communities located in Hopelchen County, where previous data indicate a high rate of natural infection of the *T. dimidiata* [13]. The Xcalot-Akal community (longitude 89.818056, latitude 19.938889), which has a population of 129 inhabitants, and Xcanahaltun-Huechil (longitude 89.818889, latitude 19.995833), which has a population of 123 inhabitants. The volunteers participating in the present study included 21 and 42 inhabitants from Xcalot-Akal and Xcanahaltun-Huechil, respectively.

Blood samples were collected and cardiomyopathies were assessed by electrocardiography after obtaining data using a pre-designed questionnaire.

A homemade enzyme-linked immunosorbent assay (ELISA) and indirect immunofluorescence (IIF) standardized techniques were used [6] to detect IgG specific for *T. cruzi*. In brief, for ELISA, the mean optical density (OD) of seronegative healthy individuals plus three standard deviations was fixed to set the cut-off (mean+3SD), serum dilution was 1:400 and incubation time for 1 h at 37°C; conjugate anti-human IgG-peroxidase 1:5000 for 1 h at 37°C. The reaction was developed for 10 min using O-fenilen-diamine and H_2O_2. For IIF, human test and control sera were diluted to 1:50 (cut-off dilution). Fluorescence of the parasites at the cut-off dilution indicates positivity. Positive and negative controls were included in all assays. In sera positive for IgG, we detected IgG1, IgG3 and IgG4 subclasses specific for *T. cruzi* [14]. The electrocardiogram (ECG) study was carried out with a portable electrocardiograph (Fukuda Denshi FX-2111) device. The ECGs were then analysed by a cardiologist, and special attention was given to rhythm, conduction and ischemia findings.

At the General Hospital of Specialties "Dr Javier Buenfil Osorio" (HGE) in Campeche City, Mexico, which serves patients from Campeche State and surrounding states, we studied 233 consecutive patients in cardiology, internal medicine and emergency units (from July 2013 to June 2014). Patients with an altered ECG or cardiac failure and co-morbidity, such as diabetes mellitus and hypertension, were included in the study for searching anti-*T. cruzi* antibodies. The present study is considered of low risk according to "Reglamento de la Ley General de Salud; National Secretary of Health Mexico". Written informed consents were obtained from all participants. The study was approved by the Research and Bioethical Committee of Universidad Autonoma de Campeche and the HGE.

Descriptive statistics consisted in mean, SD, rates, and percentage. Sample size was calculated using confidence level 95%, confidence interval between 12 to 19.6. For a population of 123 the size sample was 42 and for a population of 129 the sample was 21.

Results

In Xcalot-Akal, 9.5% (2/21) of volunteers were IgG-positive for *T. cruzi*. Their mean age was 33.5+/-12.4 SD years old, with a range between 16 and 60 years old.

In Xcanahaltun-Huechil, 2.3% (1/42) of volunteers were positive. Their mean age was 29.5+/-14.3 SD years old with a range between 5 and 71 years old. Two positive subjects were 21 years old while the third one was 37 years old; none of them presented ECG alterations. However, in the Xcalot-Akal community, ECG alterations in seronegative subjects included left ventricle hypertrophy (23.8%; 5/21) and left anterior branch blockage (4.7%; 1/21). This alteration is compatible

Table 1. Main electrocardiographic findings in two Mayan communities

Findings	**Xcalot-Akal n (%)**	**Xcanahaltun-Huechil n (%)**
Left ventricular hypertrophy	5 (23)	3 (7)
Right ventricular hypertrophy	0 (0)	8 (19)
Rhythm/conduction abnormalities	1 (5)	7 (16)
Normal electrocardiogram*	14 (66)	27 (64)
Total	21	42

* Three seropositive subjects for anti-*T. cruzi* antibodies showed normal electrocardiogram

Table 2. Main clinical diagnosis in 233 patients admitted to Regional Hospital (Hospital General de Especialidades "Dr Javier Buenfil Osorio" Campeche, Mexico)

Findings	Number of cases (%)
Systemic arterial hypertension	151 (65)
Diabetes	48 (20)
Rhythm/conduction abnormalities	45 (19)
Hypertrophic cardiomyopathy	23 (10)
Heart attack/Ischemia	18 (8)
Dilated cardiomyopathy	14 (6)*
Total	233

* One patient (7%) with dilated cardiomyopathy patients showed anti-*T. cruzi* specific IgG antibodies

with hypertension or ischemic events, but not with Chagas disease. In Xcanahaltun-Huechil, ECG alterations in seronegative subjects included right ventricular hypertrophy (19%; 8/42), and conduction system alteration (11.9%; 5/42), and sinus bradycardia (4.7%; 2/42) (Table 1). A remarkable finding is that 90% of the population recognized the vector and 65% of them had experienced contact with triatomine bites. The overall seroprevalence was 4.7% (3/63) in rural communities.

The occurrence of CCC at the Regional Hospital in 233 studied patients with an altered electrocardiogram or cardiac failure attending over one year represented 0.4% (1/233).

Arterial systemic hypertension was the most frequent pathology (65%; 151/233), and the less frequent was dilated myocardiopathy (DMC) (6%; 14/233). In this group of DMC 7% (1/14) was diagnosed as having CCC (Table 2). According to geographical origin, 42% (98/233) of patients were from urban area of Campeche State, this population are in lower risk to get infected with *T. cruzi* comparing to 30% (70/233) of patients from rural areas. An interesting finding was that 25% (18/70) of patients from rural areas come from the same area of the Mayan communities here studied.

An interesting finding is that the four positive sera showed low titers of IgG anti-*T. cruzi* antibodies. The subclass of specific IgG anti-*T cruzi* in asymptomatic subjects was preferentially IgG4 and IgG3 while in CCC patient showed a high IgG1 titer (Table 3).

Discussion

In spite of high abundance of triatomine vectors reported in the Yucatan Peninsula of Mexico, our data indicate low prevalence of human infection among inhabitants of rural communities (4.7%). This finding is in accordance with recently published studies from other rural communities in Yucatan which estimate seroprevalence of 2.3% [7–8]; however, the seroprevalence was lower in urban areas (0.1%) [4,6]. This low seroprevalence could be explained by the fact that *T. dimidiata*, the main vector in Yucatan, has a long defecation time after meals and low metacyclogenesis [15]. These two factors can influence the transmission of *T. cruzi*. In addition to probability of transmission is very low 9×10^{-4} per contact with an infected vector for transmission to human [16].

Our findings are also consistent with those from Ecuador, where high infection rates of *T. dimidiata* are associated with low rates of *T. cruzi* seroprevalence [17]. In contrast, high seroprevalence of *T. cruzi* antibodies up to 66% was reported among rural communities hyperendemic with Chagas disease in Bolivia, where (13.8%; 55/398) of patients had ECG findings suggestive of Chagas cardiomyopathy [18]. In our study, however, none of the infected subjects presented with findings compatible of Chagas disease. This could be attributed to the very small sample size of

Table 3. IgG subclasses in chronic chagasic cardiomyopathy and asymptomatic subjects

Diagnosis (age)	IgG whole (cut-off OD=0.14)	IgG1 (cut-off OD=0.12)	IgG3 (cut-off OD=0.18)	IgG4 (cut-off OD=0.5)
CCC+ (58 years old)	**0.70**	**0.50**	**0.19**	0.32
Asymptomatic Xcalot 1 (21 years old)	**0.32**	0.08	0.09	**0.72**
Asymptomatic Xcalot 2 (21 years old)	**0.58**	0.11	**0.6**	**1.74**

+ Chronic chagasic cardiomyopathy; significant titers are in bold

our study or because they were young people and disease progression is manifested in the fourth or fifth decade of life.

The CCC in patients admitted to the Regional Hospital during the study period was very low (0.4 %; 1/233). The patient presented severe conduction system alteration with ventricular arrhythmia but without dilation of heart chambers. The patient required a pacemaker device. It is known that main clinical manifestation in CCC is conduction and rhythm defects with dilatation of ventricle in advanced state of the disease. Because patients with altered ECG or cardiac failure were included in our study, the most frequent pathology detected was hypertension and diabetes whereas dilated cardiomyopathy was the least frequent pathology.

The titers of anti-*T. cruzi* specific IgG in positive subjects were low, resembling those of people living in low endemic areas [19]. This could be explained by the fact that reinfection rates are probably low in contrast to high endemic regions. The dominant IgG subclass in the CCC patient was IgG1 whereas IgG4 and IgG3 were observed in asymptomatic subjects. It has been shown that IgG1 and IgG2 titers are often high in CCC [14].

In conclusion, the present study reveals that *T. cruzi* infection has a low prevalence in rural communities of Yucatan Peninsula of Mexico, with a low impact in inducing CCC. But this does not mean however, Chagas disease should be considered in diagnosis, and vector surveillance with health education programmes in rural communities should be strengthened.

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