Acta Tropica 111 (2009) 51–55

Contents lists available at ScienceDirect

Acta Tropica

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

Clinical profile of *Trypanosoma cruzi* infection in a non-endemic setting: Immigration and Chagas disease in Barcelona (Spain)

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ARTICLE INFO

Article history:
Received 4 September 2008
Received in revised form 14 January 2009
Accepted 23 February 2009
Available online 5 March 2009

Keywords:
Chagas disease
Immigration
Cardiac disease
Trypanosoma cruzi

ABSTRACT

Background: Chagas disease is no longer limited to Latin America and is becoming frequent in industrialised countries in Europe and United States.
Methods: A descriptive study of Latin American immigrants in Barcelona attending two centres for imported diseases during a period of 3 years. The main outcome was the identification of *Trypanosoma cruzi*-infected individuals in a non-endemic country and the characterization of their clinical and epidemiological features.
Results: A total of 489 Latin American patients participated in the study. Forty-one percent were infected by *T. cruzi*, and the most frequent country of origin was Bolivia. All *T. cruzi* infected patients were in chronic stages of infection. 19% of cases had cardiac disorders and 9% had digestive disorders.
Conclusions: A high percentage of participants in this study were infected by *T. cruzi* and various factors were found to be associated to the infection. It is important to improve clinical and epidemiological knowledge of *T. cruzi* infection in non-endemic countries and to develop appropriate screening and treatment protocols in these settings.

1. Introduction

Chagas disease is a zoonosis endemic to Central and South America (Prata, 2001; WHO, 2002). Current data indicate that between 8 and 10 million people are infected in this area (OPS, 2006; CDC, 2007).

Trypanosoma cruzi, its causal agent, is a flagellated protozoan that can easily be isolated from the blood in acute infections (Prata, 2001; Sartori et al., 2007). In endemic areas, *T. cruzi* infection usually occurs after contact with the faeces of blood-sucking triatomines (Prata, 2001). Congenital, organ transplantation and transfusion-related transmission are the other principal routes of *T. cruzi* infection (Prata, 2001; Kirchhoff, 1993).

After being infected, patients may enter an acute stage of the disease that is frequently asymptomatic (Prata, 2001; WHO, 2002). This stage may also include acute myocarditis or encephalomyelitis and in 5–10% of cases can provoke death (Prata, 2001). After the acute stage the infection usually becomes chronic and clinically silent. At this point it is described as the indeterminate form (Prata, 2001). 10–30 years later, around half of infected people will develop symptomatic chronic Chagas disease, which is characterized mainly by cardiac and gastrointestinal disorders (Prata, 2001). Cardiac involvement is the main cause of death in this chronic stage (Punukollu et al., 2007). Arrhythmias, heart failure and sudden death are the most threatening complications of this infection. In endemic areas approximately 15–20% cases of infection involved the digestive tract, mainly as mega gastrointestinal syndromes (Prata, 2001).

Currently, this infection is no longer limited to the Americas since the number of immigrants from Latin America is increasing both in North America and Europe (Schmunis, 2007). Consequently, non-vectorial transmission such as congenital, organ transplanta-

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doi:10.1016/j.actatropica.2009.02.005

tion and transfusion transmission have been described in these areas (Muñoz et al., 2007; Riera et al., 2006; CDC, 2006; Flores-Chávez et al., 2008).

Schmunis et al. estimated that approximately 12,000 out of 400,000 Latin American immigrants living in Spain in 2003 were infected by *T. cruzi* (Schmunis, 2007). By 2007, the number of immigrants from Latin America had increased to 1,600,000 (INE, 2008) and, if the prevalence of infection remains similar, approximately 40,000 of these immigrants are likely to be infected by *T. cruzi*.

The clinical and epidemiological profile of Chagas disease in non-endemic countries is not well described. An improved understanding of these characteristics may help to improve the diagnosis and management of affected populations in industrialized countries (CDC, 2007; Gascón, 2005; Gascón et al., 2007). Therefore, the aim of this paper is to describe the clinical profile of a series of Latin-American at-risk population that attend the specialised centres for imported infectious diseases in Barcelona.

2. Methods

2.1. Design and setting

This study was performed in the two centres for imported diseases in Barcelona: Unitat de Medicina Tropical i Salut Internacional Drassanes, which is a Primary Care Centre, and the Centre for International Health, in the Hospital Clínic, a University hospital.

This was a descriptive study of 489 adult Latin American immigrants attending these two centres for imported diseases over a period of 3 years.

2.2. Recruitment and participants

All participants were of Latin American origin, from *T. cruzi* endemic areas and had come to the clinics between July 2004 and July 2007. Regardless of the reason for their visit, patients were invited to participate in the study, after obtaining informed consent.

Clinical and epidemiological data were obtained, which included age, clinical symptoms, country and area of origin, history of rural environments and mud houses, pregnancy, and finally, their history of blood donation or transfusion.

For laboratory diagnosis, two serological ELISA tests were performed following international recommendations (WHO, 2002). One was a commercial ELISA with recombinant antigens (BioELISA Chagas®, Biokit S.A., Lliçà dĭ Amunt, Barcelona, Spain), and the second was an in-house ELISA with whole *T. cruzi* epimastigotes antigen. For discordant tests we used a Western blot technique, with antigen from *T. cruzi* epimastigotes. Participants were considered infected if the results from two serological methods were positive (WHO, 2002). Blood nested-PCR (Marcon et al., 2002) and real time-PCR (Piron et al., 2007) were performed for seropositive participants. Nested PCR was carried out at the beginning of the study. This was later substituted by a real-time PCR that amplifies the same DNA region as the nested-PCR, but is safer and easier to perform, while giving similar results (Piron et al., 2007).

T. cruzi infected patients were studied using a protocol that included a 12-lead electrocardiogram (ECG), chest X-ray, haematology, biochemistry, and HIV serology. ECG was interpreted by a single reader. Suspicion of cardiac involvement was based on the presence of any of the clinical or ECG criteria shown in Table 1 (Gascón et al., 2007).

Echocardiography was performed on patients in whom cardiac involvement was suspected. Systolic dysfunction was defined as an ejection fraction below 60%.

A barium X-ray of the colon and oesophagus was performed in patients complaining of gastrointestinal symptoms. Patients with disorders of the oesophagus were classified following the classical description of Rezende, which classifies the oesophageal aperistalsis into four groups I–IV (de Rezende et al., 1960). The colon was considered abnormal when the sigmoid diameter was over 6 cm (Ximenes, 1984). Other examinations were performed according to different clinical signs and symptoms reported by patients.

Table 1
ECG and clinical criteria for suspicion of cardiac involvement (modified from Gascón et al., 2007).

ECG criteria
Bradycardia <50 bpm: AV block, any type of bundle branch block or hemiblock, ventricular premature beats, tachyarrhythmia of any origin, q-waves suggestive of necrosis and T-waves changes suggesting ischemia.
Clinical criteria
Dyspnea, ortopnea, and signs of congestion.
Syncope, dizziness and palpitations.
Chest pain suggesting coronary heart disease.

T. cruzi infected patients were classified into the indeterminate, cardiac, digestive, and mixed clinical forms of Chagas disease. We defined the indeterminate form when a seropositive patient had no evidence of cardiac or gastrointestinal tract involvement. Specific treatment with benznidazole was offered to all infected participants.

2.3. Statistical analysis

We analysed the associated variables with *T. cruzi* using Fisher's exact test in the categorical data variables. If the variables were continuous, the Wilcoxon rank sum test was used. To quantify the ratio/association of these variables with *T. cruzi*, univariate and multivariate Logistic Regression Models were estimated. Odds ratio (OR) and 95% confidence interval were calculated. Statistical tests were performed using a two-sided significance level of 0.05. Software for analysis was STATA 9.0 (StataCorp. 2005, Stata Statistical Software: Release 9.0. College Station, TX: StataCorp. LP.).

3. Results

A total of 489 Latin American patients from 14 different countries were included in the study (Table 2). A total of 202 (41%) participants were infected, and 14 (7%) of them had received blood transfusions in their country of origin. PCR was performed on 200 of the infected patients, and was positive in 56 patients (28%). Eleven participants were pregnant women and three of them were infected with *T. cruzi*. All three mothers and newborns were asymptomatic. Table 3 shows the basic epidemiologic characteristics according to infection status.

Table 2
Distribution of *T. cruzi* infected people by country of origin.

Country of origin	*T. cruzi*-infected, *N* (%)	Total, *N*
Bolivia	175 (65%)	269
Ecuador	3 (3%)	101
Colombia	2 (7%)	29
Perú	3 (16%)	19
Argentina	10 (56%)	18
Brasil	2 (14%)	14
Honduras	2 (14%)	14
Paraguay	2 (33%)	6
Venezuela	1 (20%)	5
Nicaragua	0	4
Chile	2 (50%)	4
Uruguay	0	3
Mexico	0	2
El Salvador	0	1