Original Article

Seroprevalence and vertical transmission of Chagas disease in a cohort of Latin-American pregnant women in a tertiary hospital in Madrid

Laura Francisco-González a,*, Teresa Gastañaga-Holguera b, Beatriz Jiménez Montero a, Zarife Daoud Pérez a, Marta Illán Ramos a, Paloma Merino Amador c, Miguel Ángel Herráiz Martínez b, José Tomás Ramos Amador a

a Department of Paediatrics, Hospital Clínico San Carlos, Madrid, Spain
b Department of Obstetrics and Gynaecology, Hospital Clínico San Carlos, Madrid, Spain
c Department of Clinical Microbiology, Hospital Clínico San Carlos, Madrid, Spain

Received 9 October 2016; accepted 4 March 2017

Keywords
Chagas disease; Vertical transmission; Prenatal screening

Abstract

Background: Chagas disease, caused by Trypanosoma cruzi (T. cruzi), is endemic in Latin-America and is emerging in Spain due to immigration. The vertical transmission rate is around 5%. A routine prenatal screening with serology of all pregnant women from endemic areas is recommended to identify infected newborns, allowing early treatment and cure.

Objective: The aim of this study was to estimate the prevalence of positive Chagas serology in a cohort of pregnant women from Latin-America and its vertical transmission.

Patients and methods: An observational, prospective, follow-up study was conducted on women with positive serology to T. cruzi, as well as their newborns, from January 2013 to April 2015. Congenital Chagas was ruled out using a PCR technique at birth and at 1 month, and with serology at 9–12 months old. A child was considered infected when PCR was positive, and uninfected when PCR was negative, and/or it had a negative serology.

Results: Screening was performed on 1,244 pregnant women from Latin-America, and there were positive results in 40 (prevalence 3.2%, 95% CI: 2.4–4.4%), with 85% of them from Bolivia.

© 2016 Asociación Española de Pediatría. Published by Elsevier España, S.L.U. All rights reserved.
There was only one infected newborn (rate of vertical transmission 2.8% (95% CI: 0–15%)), who had a positive PCR at birth. Relative studies enabled an 8-year-old sister with an asymptomatic disease to be diagnosed and treated. Both were treated successfully with benznidazole (later the PCR and serology were negative).

**Conclusion:** Screening during pregnancy in Latin-American women helped to detect those with Chagas disease. The rate of vertical transmission was 2.8%, in keeping with literature. Screening led to the detection and treatment of previously unidentified familial cases.

© 2016 Asociación Española de Pediatría. Published by Elsevier España, S.L.U. All rights reserved.

---

**Introduction**

Chagas disease, which is caused by the protozoan *Trypanosoma cruzi* (*T. cruzi*), is endemic in Central and South America (with the highest prevalence in Bolivia) and emerging in Spain and other European countries in association with the immigration of individuals from endemic areas to these countries.

The main mode of transmission in endemic areas is vector-borne (triatomine bugs), but there are other routes of infection (ingestion of contaminated foods, blood transfusions, organ transplants and vertical transmission). Vertical transmission (whose prevalence is estimated at approximately 5% of newborns of infected mothers in endemic areas and 2–3% in non-endemic areas) is the most frequent mode of transmission in Spain.

Selective screening of pregnant women is recommended for the subsequent identification of infected infants, which allows early treatment (better tolerated in the paediatric population) and cure of the disease.

The aim of this study was to estimate the prevalence of positive serologic test results for Chagas disease in a cohort of Latin American pregnant women followed up in our hospital to establish the rate of vertical transmission.

**Patients and methods**

We conducted a prospective observational study by following up a cohort of pregnant women with positive serological tests for *T. cruzi* and their newborns in a tertiary hospital in Madrid between January 2013 and April 2015.
Screening for Chagas disease (ELISA for *T. cruzi* [ARCHI-
TECT Chagas Abbott]) was performed in all pregnant women
from endemic areas (between Mexico and Argentina, with
the exception of the Caribbean islands) in the first trimester
of pregnancy. In women that tested positive, the result
was confirmed by immunochromatography (SD BIOLINE rapid
Chagas Ab test). Women with positive serologic test results
were referred to the Tropical Medicine clinic for follow-up
and treatment planning.

The follow-up of infants conforming to the consen-
sus protocol of the Sociedad Española de Infectología
Pediátrica, Sociedad Española de Enfermedades Infecciosas
y Microbiología Clínica and Sociedad Española Ginecológica
y Obstetricia (Spanish Societies of Paediatric Infectious
Disease, Infectious Disease and Clinical Microbiology, and
Gynaecology and Obstetrics), which call for performance of
PCR at birth and 1 month of life, and serologic testing at
birth and 9–12 months of life.

We considered infants with a confirmed PCR infected,
and infants with 2 negative PCR results (at birth and at
4–8 weeks) or with a negative PCR and disappearance of
previously detected antibodies not infected.

Results

During the period under study, 1,244 pregnant women from
Latin America (78% of the all pregnant women from this
region) underwent screening for *T. cruzi*, of who 40 had
positive results (prevalence, 3.2%; 95% confidence inter-
val [CI], 2.4–4.4%). Of those with positive serologic test
results, 85% were from Bolivia, 10% from Paraguay, 2.5% from
Ecuador and 2.5% from Argentina. The prevalence in Bolivian
pregnant women was 16.3% (95% CI, 12.6–20.8%).

We identified 40 infants born to mothers with positive
test results for Chagas disease. Infection was confirmed
at birth in only one infant (vertical transmission rate, 2.8%
(95% CI, 0–15%), born to a Bolivian mother aged 36 years with
Chagas disease in the chronic indeterminate phase (asym-
ptomatic). This infant had a case of symptomatic congenital
Chagas disease (hydrops fetalis, ascites, haemodynamic
instability, anaemia) and required admission to the neonatal
intensive care unit. The patient had a positive PCR result at
birth, and responded favourably to a 60-day course of treat-
ment with benznidazole (initial dose of 5 mg/kg/day, raised
to 8 mg/kg/day in the second week after ensuring absence of
adverse events) that was well tolerated, with resolution of
symptoms and negative results of a second PCR assay (at
age 3 months) and serologic testing (at age 9 months).

All the identified infants (with the exception of the case of
vertical transmission) had negative PCR assays at birth and
were followed up in adherence to the current protocal,
with negative results of an additional PCR assay at 4 weeks
and evidence of clearance of antibodies between 9 and 12
months. In our hospital, we did not perform microscopic
examination of a blood smear at birth and age 1 month on
account of its low sensitivity and the availability of PCR. In
75% of the infants (30), the follow-up was completed, with
confirmation of absence of antibodies by serologic testing;
in 87.5% (35) at least 2 PCR assays or 1 PCR assay and 1 sero-
logic test at age 9–12 months were performed whose results
were negative; while 12.5% patients (5) only had negative
results in an initial PCR assay at birth, and were therefore
considered lost to follow-up.

The identification of infected pregnant women through
positive serologic tests also allowed us to evaluate the
siblings of their newborns, which led to the diagnosis of
another asymptomatic case of Chagas disease in a girl aged
8 years (from Bolivia) that had not been detected at birth.
She underwent treatment with benznidazole (at a dose of
10 mg/kg/day for 60 days) and was tested at regular
intervals, tolerated the treatment well, and had a good out-
come with eventual disappearance of antibodies (6 months
after completing treatment). The remaining members of
the household were evaluated at the Tropical Medicine clinic.

Discussion

The selective screening of pregnant women from Latin
America in our hospital allowed us to identify those who
had Chagas disease, evincing a high prevalence among those
from Bolivia.

The rate of vertical transmission in our cohort was 2.8%
(95% CI, 0–15%), consistent with the data reported in the
literature. Few data have been published for non-endemic
regions, but there is evidence of a lower rate of vertical
transmission, which is probably due to pregnant women usu-
ally being in the chronic phase of disease, when parasite
loads are lower.

Furthermore, screening of pregnant women allowed us
to extend the evaluation to the rest of the household, with
the detection and treatment of cases that had not been
identified at birth. Thus, we were able to make an early
diagnosis in paediatric cases, including cases in the asym-
ptomatic phase, preventing complications and achieving cure
of the disease.

Identification of infection in this cohort of pregnant
women also allowed the follow-up of those infected, to
whom we recommended starting treatment (if they had not
already received it) once they stopped breastfeeding.

Vertically-transmitted congenital Chagas disease is usu-
ally asymptomatic (70–80% of cases). There is variability in
the clinical presentation of patients who are symptomatic
at birth, usually with involvement of several organs and
systems as was the case of the sole case of vertical trans-
mision identified in our cohort, which we have discussed in
a previous publication.

In newborns, a positive serologic test is no proof of infec-
tion, as it can also result from the placental transfer of
maternal antibodies (IgG), so the diagnosis should be based
on methods for parasite detection (PCR or blood smear
eamination), which we recommend performing at birth and
repeating at age 1 month due to the possibility of false neg-
ative results (as their sensitivity depends on the level of
parasitaemia). In Spain, the use of PCR is recommended due
to its higher sensitivity compared to blood smear (observa-
tion of the parasite by microscopic examination the smear).
The sensitivity of PCR is high during the acute phase (up to
90–95%) and decreases during the chronic phase of disease
(ranging between 50% and 80% in different case series);fur-
thermore, it has a specificity of nearly 100%. 
Nevertheless, microscopic examination of blood smears continues to
be useful in endemic areas, where molecular techniques
such as PCR are less frequently available in laboratories, and its sensitivity depends on the experience of the individual performing the examination. While the yield of parasite detection methods is higher in children compared to adults because children are usually in the acute phase of disease and have higher parasite loads, confirmation of the disappearance of antibodies by serologic testing is recommended starting at age 9 months, although antibodies may not actually become undetectable until age 12 months. From age 9 months, the persistence of antibodies without a decrease in their titre is indicative of infection. In our cohort, serologic testing was performed between the ages of 9 and 12 months and was negative in all uninfected patients, who all had negative results in preceding PCR assays (we did not detect any false negatives of PCR). In children aged more than 12 months, as in adults, serologic testing is the gold standard for diagnosis, and positive results should be confirmed by performance of a different serologic test.5

When it comes to treatment, two drugs are currently authorised for Chagas disease: benznidazole (the treatment of choice) and nifurtimox (alternative treatment).10,11 A paediatric formulation is not available for either. Clinicians should be aware that adverse reactions are less frequent and treatment is therefore better tolerated before age 7 years.12 The data currently available do not suffice to determine the mechanism by which toxicity increases with age. It is believed that it involves increasing plasma concentrations of the drug, as the clearance rate is higher in children and results in a shorter half-life, which suggests that reducing the dose in adults to achieve concentrations similar to those found in children could reduce toxicity without affecting the effectiveness of treatment.13

The recommended dosage of benznidazole is 8–10 mg/kg/day administered in 2 doses for 60 days (it is the same for children and infants, except for preterm infants or patients with a concurrent disease in whom a lower initial dose of 5 mg/kg/day is recommended, with increases starting 1 week after if the patient tolerates the drug well and laboratory tests results are normal until a dose of 8–10 mg/kg/day is reached).5 The results of studies conducted in recent years in children as well as adults with Chagas disease in highly-endemic countries suggest that we should consider reducing the dose of benznidazole or the duration of treatment, as such reductions have not been associated with a decrease in efficacy.14,15

In the case of nifurtimox, which is usually prescribed in patients with poor tolerance of benznidazole, the recommended dosage is 15–20 mg/kg/day given in 4 doses for a period of 90 days.5 These drugs may cause adverse reactions, most frequently gastrointestinal, cutaneous and haematologic, which requires close monitoring of patients (including clinical manifestations and laboratory parameters) during treatment and the month following its completion. In our study, none of the 2 paediatric patients treated with benznidazole experienced adverse events.

One of the limitations of our study is that due to the small sample size, the CI of the estimated vertical transmission rate was very wide. Performance of multicentre studies or studies with a longer period of follow-up would be advisable for the purpose of obtaining a larger sample size and thus more conclusive results. Furthermore, we could not rule out vertical transmission in 5 patients who were lost to follow-up and who had a single negative result of PCR at birth. In one case, this was due to the death of the patient before the end of the study (due to disseminated tuberculosis), and in the rest, to patients not coming to the scheduled follow-up appointments. Since the population of interest is a population of immigrants, there are barriers to long-term follow-up, including the potential return to the country of origin.

To conclude, we ought to underscore that systematic screening of the at-risk population (pregnant women or children from endemic areas) is justified, as this disease has a silent course in a considerable percentage of patients (especially during the acute phase) and can be vertically transmitted, so that failure to perform screening may result in a delayed diagnosis. Based on our results, we believe that screening should be performed systematically in all patients coming from Bolivia, given the high prevalence of Chagas disease in this country, but also indicated in patients from any other Latin American country, among who cases also occur, in order to ensure early diagnosis and minimise the risk of complications.

Furthermore, treatment in newborns achieves a high cure rate (of nearly 100%) with a low associated toxicity, while the probability of adverse events increases and the probability of success decreases with the age of the patient.12

Conflicts of interest

The authors have no conflicts of interest to declare.

References