

# Congenital transmission of *Trypanosoma cruzi* in central Brazil. A study of 1,211 individuals born to infected mothers

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*Transmission of Trypanosoma cruzi during pregnancy is estimated to occur in less than 20% of infected mothers; however, the etiopathogenesis is not completely understood. The Centre for Studies on Chagas Disease provides confirmation of T. cruzi infection for individuals living in central Brazil. In this retrospective hospital-based study, all requests for diagnosis of T. cruzi infection in individuals less than 21 years old from 1994-2014 were searched. We end with 1,211 individuals and their respective infected mothers. Congenital transmission of infection was confirmed in 24 individuals (2%) in central Brazil, an area where the main T. cruzi lineage circulating in humans is TcII. This low prevalence of congenital Chagas disease is discussed in relation to recent findings in the south region of Brazil, where TcV is the main lineage and congenital transmission has a higher prevalence (approximately 5%), similar to frequencies reported in Argentina, Paraguay and Bolivia. This is the first report to show geographical differences in the rates of congenital transmission of T. cruzi and the relationship between the prevalence of congenital transmission and the type of Tc prevalent in each region.*

Key words: Chagas disease - *Trypanosoma cruzi* - congenital transmission - geographical differences - familial studies

Perinatal transmission of *Trypanosoma cruzi* is estimated to occur in a low percentage of infected mothers (less than 20%); the reasons for the low prevalence of this route of transmission are not clearly understood. Few large studies are available and those that have been conducted are mainly from three countries: Argentina, Bolivia and Paraguay, where the congenital transmission rate is 5% (4.1-6%) (Howard et al. 2014). Currently, as a consequence of migration, Chagas disease is widespread, mainly in some countries of Europe and the United States of America (USA). Congenital transmission has accompanied this migration, but has mainly been observed in Spain (Barona-Vilar et al. 2012) and Switzerland (Jackson et al. 2009) among almost exclusively Bolivian mothers; congenital transmission rates, as expected, are similar to Bolivian estimates. It is noteworthy that few cases of congenital transmission have been reported from the USA, even though the number of infected immigrants to the USA, mainly from Mexico, is higher than in Spain (Schmunis 2007).

In Brazil, several surveys have been performed [reviewed recently by Martins-Melo et al. (2014)] and figures are consistently lower than those found in other South Cone countries, with a rate of approximately

1%. The reasons for this variation have not yet been explained. A recent survey has shed some light on this subject; a study of more than 100,000 samples from children younger than five years old, which covered all areas of Brazil (Luquetti et al. 2011) except the state of Rio de Janeiro (RJ), aimed to detect vector-borne transmission after insecticide spraying performed before these children were born. As a secondary result of this study, 20 congenital cases were found, 60% of which were from the state of Rio Grande do Sul (RS). In this region of Brazil, a different lineage of *T. cruzi* is prevalent (TcV), making this area similar to those previously cited countries where the same type of *T. cruzi* is also prevalent and a higher transmission rate (5%) has been reported.

In our view, these data support the existence of decisive geographical differences in *T. cruzi* transmission. Specifically, the supporting data include the large numbers of infected mothers in regions where TcV is prevalent, who experience an average transmission rate of 5% (4-6%) and the low numbers of infected mothers in Brazil, which experiences a lower congenital transmission prevalence of approximately 1%. Additional supporting data are the low number of cases reported in Mexico and the USA despite the presence of a large number of infected women of childbearing age, as well as the recent finding of striking differences within Brazil, with five-10 times more congenital cases occurring in a single state where a different Tc lineage is prevalent than in any other region.

The objective of this report is to ascertain the transmission rate of *T. cruzi* in children born from mothers who acquired the infection in central Brazil, an area of high TcII prevalence, to reinforce the data of the recent serological survey (Luquetti et al. 2011) that found lower transmission rates in all municipalities of Brazil exception the RS.

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## SUBJECTS, MATERIALS AND METHODS

**Sample population** - This hospital-based study was performed using the database from the Chagas disease laboratory of the Centre for Studies on Chagas Disease (NEDoC), which started in 1978 and provides clinical and laboratory diagnoses for this infection. The population referred to NEDoC for diagnosis derives from the Clinics Hospital [a teaching hospital at the Federal University of Goiás (HC-UFG), Brazil], blood banks in the state of Goiás (GO), private practices and a screening program for all pregnant women living in GO (operating since 2004) (Botelho et al. 2008, Gomes Filho et al. 2009, Siriano et al. 2011). In this screening program, all pregnant women confirmed to be positive for Chagas disease are requested to bring their child for testing six months after birth. In addition, all women with confirmed infections who have children are also requested to bring them to be tested for Chagas disease (Carlier et al. 2011). All serum samples are subjected to either three or four conventional serological tests: indirect immunofluorescence (IIF) (in house with BioMérieux conjugate, France), indirect haemagglutination (IHA) (Wiener, Argentina), ELISA (Biomanguinhos-Fiocruz, Brazil) and ELISA (Grupo Bios, Chile). Samples are stored indefinitely in frozen aliquots (at -20°C) and thawed when needed.

**Selection of sera** - We searched our records of 20,667 sera for those belonging to individuals less than 21 years old that were seen between November 1994-October 2014 and we identified 2,167 sera fitting these criteria. This period corresponds to the start of the NEDoC out-patient clinic. Subsequently, we linked the cases to their respective mothers and found 1,361 case-mother pairs. Pairs were excluded if they had any of the following: mother with negative serology ( $n = 74$ ), mother with dubious serology ( $n = 10$ ), mother already given specific treatment ( $n = 4$ ), child from whom we had only a sample of cord blood or blood collected before six months of age ( $n = 44$ ), child with positive serology who lived in an endemic area where vector transmission could not be ruled out ( $n = 14$ ) or child who received a blood transfusion ( $n = 3$ ). After the exclusions, we had 1,211 pairs of sera from children and their mothers with confirmed infections.

Exclusion of 150 pairs did not modify the profile of the case population, which had a mean age of 7.4 years and was 50.7% male.

For cases where the diagnosis was unclear, an aliquot of serum was separated and all serologic tests were repeated. Inconclusive serology was defined as results including one or more positive test, one or more negative test and one or more borderline test.

Diagnosis of congenital transmission was made either by direct parasitological methods (in the newborn) or by positive serology of all four tests after four months of age. Exclusion of congenital transmission was determined by a negative serology at any age from a child/young adult born from a mother with confirmed infection.

All mothers completed a questionnaire, which collected information on the municipality where each mother was born and the subsequent places where they lived.

**Statistical analysis** - We provide descriptive statistics for population characteristics and the frequency of congenital transmission. Comparison of categorical variables was performed by Pearson's  $\chi^2$  test. Continuous variables were compared using Student's  $t$  test. In all statistical tests, the alpha error level was set at 5%.

**Ethics** - Institutional Review Board approval was obtained for all study procedures at the HC-UFG.

## RESULTS

**Family study** - After exclusions, though some mothers' infections were not obvious, 1,211 pairs of individuals less than 21 years old and their mothers, who were proven to be infected by four different serological tests, were found.

There was no predominant sex among the young individuals (591 male and 573 female) and their mean age was 7.4 years old (age range: 110 days - 20 years old). The distribution of age is shown in Table I. In 23 cases, the sex of the child was not determined because the samples were received with only the name of the mother (i.e., "newborn of MMS"). These children were not seen again at the NEDoC.

**Children without transmission** - In 1,187 samples from children, serological results were negative. These

TABLE I

Children: distribution by age - Clinics Hospital, Federal University of Goiás, Goiânia, Goiás, Brazil, 1994-2014

Age group (years)	No transmission			Transmission			Total
	Children/young adults (n)	Gender F/M (n)	Mean age (years)	Congenital transmission (n)	Gender F/M (n)	Mean age (years)	
0-1	266	107/136	0.7	4	1/3	0.4	270
1.1-12	610	306/304	6.3	9	5/4	4.8	619
13-20	311	160/151	15.1	11	6/5	17.5	322
Total	1,187	573/591	7.4	24	12/12	9.9	1,211

F: female; M: male.

results were stratified by age into newborns (< 1 year old), children (up to 12 years old) and young adults (13-20 years old) (Table I).

Among the newborns (n = 266), a second collection of blood was required in 71 individuals because the serum was from cord blood or was taken before six months of age. It should be emphasised that all blood collected before six months of age showed antibodies against *T. cruzi*, even in cases where the antibodies disappeared in a later, second collection of blood. Therefore, passive transference was demonstrated. This was clear from the high antibody titres in blood taken at one-two months of age. In some cases, if the first collection was at three-four months, one or more serological reactions was negative or inconclusive, indicating a decay in antibody titres, which was confirmed on a second collection of blood after six months of age. As already explained, mothers with inconclusive serology results were excluded.

Among those children who had only a single collection taken, the youngest was 110 days of age at the collection time and two other cases were five months of age (160 and 178 days). The remaining single collection children were six months of age or older. Each of these cases was carefully evaluated to reach a definite diagnosis. For example, the youngest case (110 days of age) had two negative tests (ELISA and IHA), an IIF with a titre of 1/20 (inconclusive) and a positive Wiener ELISA recombinant test, with an index 1.2 times higher than the cut-off optical density (OD). Therefore, the overall testing results were inconclusive for this individual. However, in comparing the results with those of the mother, it was found that she had low antibody titres, as follows: ELISA 1.4 times higher than the cut-off OD, IIF 1/320, IHA 1/320 and ELISA Wiener recombinant 7.1 times higher than the cut-off OD. These titres, though low, were several times higher than those of the son; thus, we concluded that his serology was negative.

For the second group of children (1-12 years old, n = 610), a single collection of blood was enough to show no antibodies against *T. cruzi*. Most cases were clearly negative, but one of the tests occasionally showed a borderline reactivity. In four cases, one test was positive but the other three were negative, confirming the absence of specific antibodies.

For the third group of individuals (over 12 years old, n = 311), a single collection of blood was also sufficient and no cases of positivity in only one of the four tests was observed.

*Children with transmission* - Among the 1,211 pairs of individuals and their mothers, antibodies were present in 24 individuals and in their respective mothers. All of these 24 individuals lived in urban areas and had not received previous transfusions, thus they were classified as having congenital transmission of parasites from their mothers. This result indicates a 1.98% rate of transmission (Table I).

These 24 cases had mean age of 9.9 years old and 50% were female. The diagnosis was performed by the finding of parasites in two cases, one at 13 days of age and the other at 58 days of age (Table II, cases 1, 3). Interestingly, a search of parasites was performed in another 38 newborns

because they were born from infected mothers, with negative results. Later, all of these cases proved to be the result of the passive transference of maternal antibodies.

Regarding age at time of diagnosis, four cases were less than one year old, nine were one-10 years old and 11 were older than 12 years old. Other demographic characteristics, diagnostic method, mother's origin, siblings, electrocardiogram result, treatment and follow up are shown in Table II. Interestingly, two cases (cases 4, 8) were from the same mother, who was born in a different state, RS, where the prevalence of congenital transmission is apparently high. As all other mothers were born and lived in central Brazil, the real transmission rate in mothers from this region was 22 cases out of 1,209 pairs, which makes the rate of transmission for central Brazil even lower (1.8%).

Most cases were diagnosed *via* positive serology, which was confirmed by several techniques. Only two cases were diagnosed because of the presence of parasites (Table II). Newborns were sent to NEDoC by a paediatrician, whereas some of the young adults came as blood donors after being detected by screening at the blood bank. Most of the female young adults were detected by the state program for pregnant women (n = 8). Mothers of several of the congenital cases brought their other children for testing; however, most of them were not infected. The single exception was the mother born in RS, who contributed two congenital cases.

Regarding the symptoms in these individuals, most of them were asymptomatic and had normal electrocardiogram results (n = 15) (Table II). Nevertheless, severe cardiopathy was diagnosed in three individuals; two of them, aged 14 and 18 years old, later died.

Specific treatment was offered in all infected cases that returned for their results. Young adults frequently did not return and declined further follow up when contacted. Some mothers did not bring their children back or refused treatment. For those who started benznidazole, some were lost to follow up. Of the successfully treated cases, two were cured (cases 1, 7), with negative serology after four and two years of follow up, respectively. Another two treated individuals still have positive serology at high titres, even after seven and eight years after treatment.

*Mothers* - Many mothers contributed more than one child to this study. The number of individuals recorded was 1,211, but the number of mothers was 678 (Table III). Some mothers contributed up to six children. When mothers who contributed more than three children (n = 34) and their 149 respective children were excluded, the proportion of the numbers of children/mothers remained similar (1.79 and 1.65, respectively).

To determine the location of infection in the mothers, the geographical distribution of the 678 mothers was recorded. Most of them lived their childhood in the same endemic region and after reaching eight-10 years of age, moved to a large city. More mothers were born (and likely infected) in the state of Bahia (BA) (57%) than in GO (31%) (Table IV) and there were also mothers from other Brazilian states and a Bolivian mother. Interestingly, the mothers who transmitted the infection were mainly born in GO (66%).

TABLE II  
Description of 24 congenital cases, Clinics Hospital, Federal University of Goiás (NEDoC), Goiânia, Goiás (GO), Brazil, 1994-2014

Case	Date of birth	Date blood collected	Age	Sex	Diagnosis	Sent by	Mother born	Remarks	ECG	Treatment	Follow-up
1-20518	15 August 2007	28 August 2007	13 d	M	Strout	Paediatrician	Correntina BA	2 siblings negative	Normal	BZ-2007 10 mg x 60 d	4 y cured
2-19923	13 February 2007	8 May 2007	2 m	F	Serology	Paediatrician	Congenital (case 23)	1 sister normal	Normal	BZ-2010	3 y positive
3-28695	1 July 2012	28 August 2012	2 m	M	Fresh blood	Paediatrician	Canapolis BA	2 siblings negative	Normal	BZ-2012	1 y positive
4-23154	14 April 2008	16 March 2009	11 m	M	Serology	National Health Service	Caibate RS	1 sister congenital (case 8) and 1 negative	Normal	BZ-2009	Lost
5-20916	7 July 2006	8 November 2007	1 y	F	Serology	State program for pregnant	Cavalcante GO	2 siblings negative	ND	Lost	Lost
6-28221	12 February 2011	6 March 2012	1 y	F	Serology	National Health Service	São Luiz M Belos GO	1 brother negative	Normal	BZ-2012	Lost
7-10595	20 November 1998	31 October 2000	1 y 11 mo	M	Serology	Paediatrician	Dead for Chagas Disease GO	2 siblings negative	Normal	BZ-2001 5 mg x 60 d	2 y cured
8-20977	27 May 2005	21 November 2007	2 y	F	Serology	State program for pregnant	Caibaté RS	Sister of case 4	Normal	BZ-2008	Lost
9-14952	25 November 1998	13 October 2004	5 y	M	Serology	NEDoC	Carinhanha BA	2 siblings negative	Normal	BZ-2005	7 y positive
10-11635	22 January 1995	4 September 2001	6 y	F	Serology	NEDoC	Wanderley BA	1 sibling negative	Normal	BZ-2001 adverse reaction	Lost
11-14537	11 March 1997	2 July 2004	7 y	M	Serology	Paediatrician	Inhumas GO	1 sibling negative	Normal	BZ-2005	3 y lost
12-11505	2 March 1992	31 July 2001	9 y	M	Serology	NEDoC	Porangatu GO	1 sibling negative	Normal	BZ 2001	4 y lost
13-30833	27 June 2004	8 August 2014	10 y	M	Serology	State program for pregnant	Paracatu MG	ND	ND	ND	Recent
14-17888	20 July 1991	16 May 2006	14 y	M	Serology	NEDoC (cardiopaediatrician)	Formosa GO	1 sibling negative	SC	BZ-2006	Dead 2008
15-14026	15 March 1987	29 January 2004	16 y	M	Serology	NEDoC	Paráuna GO	1 sibling negative	Normal	BZ-2004	2 y lost



Case	Date of birth	Date blood collected	Age	Sex	Diagnosis	Sent by	Mother born	Remarks	ECG	Treatment	Follow-up
16-19746	20 January 1989	3 April 2007	17 y	F	Serology	State program for pregnant	Mother dead for Chagas disease	1 newborn negative	Normal	BZ refused	-
17-5878	2 September 1977	18 July 1996	18 y	M	Serology	Blood donor	Ouro Verde GO	No	SC	No	Pacemaker 1998 dead 2008
18-7891	24 July 1979	18 June 1998	18 y	M	Serology	Blood donor	Itapaci GO	No	SB	No	Lost
19-15112	21 January 1996	16 November 2004	18 y	F	Serology	NEDoC	Sancleirândia GO	No	Normal	BZ 2005	8 y positive serology indeterminate form
20-20736	15 June 1989	28 September 2007	18 y	F	Serology	State program for pregnant	Santa Terezinha GO	No	AVB	No	Lost
21-21628	31 July 1989	18 April 2008	18 y	F	Serology	State program for pregnant	Aruana GO	No	AVR	No	Lost
22-22505	8 September 1990	15 October 2008	18 y	M	Serology	Blood donor	Mother dead for Chagas disease	2 sisters negative	ND	No	Lost
23-15494	12 May 1985	18 February 2005	19 y	F	Serology	State program for pregnant	Itapaci GO	Mother of case 2	Normal	Refused	-
24-20019	26 March 1998	21 May 2007	19 y	F	Serology	State program for pregnant	Nova América GO	1 sister and 1 newborn negative	CRBBB	No	Lost

AVB: atrioventricular block; AVR: non-specific alteration of ventricular repolarisation; BZ: benznidazole; CRBBB: complete right bundle branch block; d: day; ECG: electrocardiography; m: month; ND: not done; SB: sinus bradycardia (52 bpm); SC: severe cardiopathy; y: year. Brazilian states: Bahia (BA), Minas Gerais (MG), Rio Grande do Sul (RS).

TABLE III

Number of mothers and children studied - Clinics Hospital, Federal University of Goiás, Goiânia, Goiás, Brazil, 1994-2014

Children/ mother (n)	Mothers (n)	Children (n)	Children congenital (n)
1	319	319	8
2	232	464	6
3	93	279	10 <sup>a</sup>
4	24	96	-
5	7	35	-
6	3	18	-
Total	678	1,211	24

a: two from the same mother.

## DISCUSSION

This is a detailed study of 1,211 pairs of individuals and their mothers who were serologically confirmed to be infected with *T. cruzi*. All serology was carefully performed with at least four different techniques of different principles. Inconclusive results, usually observed in 1.4% of serological tests for detection of *T. cruzi* infection (Luquetti & Schmuñis 2010), were excluded. When the concentration of antibodies was low in one of the tests, aliquots of sera were separated and all tests were performed again. There were three population groups: mothers with high antibody titres, individuals born from these mothers with a clear negative serology and a small group of 22 sera from individuals less than 21 years old with positive results and high antibody titres. In two cases, parasites

were found with direct tests; these individuals were at an age where maternal antibodies were present as well.

A questionnaire was administered to each mother at the time blood was taken at NEDoC to determine the place in which they were born, how many years they lived there and the subsequent places in which they lived, as well as the time spent in each municipality and the residence at present. From each mother, a record for the place in which they probably acquired the infection was created, chiefly considering the first 10 years of life. Most of the mothers remained in the same place during childhood (data not shown). In a few cases where mothers had not lived in endemic areas, there was a suspicion that some could have acquired Chagas disease by a congenital mechanism. In four such instances, it was possible to collect blood from the mother (grandmother of the child) and congenital transmission was confirmed (data not shown). Two of the mothers who acquired the infection congenitally contributed their own congenitally infected children, supporting the idea of second generation congenital transmission (Carlier & Truyens 2010).

From the populations with conclusive results, i.e., presence or absence of antibodies against *T. cruzi* (or parasites in 2 newborns), a group of 24 was labelled as resulting from congenital transmission. The observed rate of transmission by this mechanism was 2%. Taking into account that one mother was born in another state (RS) and contributed with two of these cases, the rate of transmission from mothers born in states other than RS, mainly in central Brazil, was 1.8%.

Studies on congenital transmission are difficult to perform because the rate is low, below 10%. Therefore, it is necessary to survey hundreds of mothers to select those infected. Study design also depends on the prevalence of Chagas infection (OMS/OPS 2006). If the expected prevalence is 5% (high), it is necessary to look for 2,000 pregnant women to find 100 infected and less

TABLE IV

Geographical origin of mothers where acquired the infection - Clinics Hospital, Federal University of Goiás, Goiânia, Goiás (GO), Brazil, 1994-2014

Origin	Main microregions <sup>a</sup>	n (%)	Congenital transmission (n)	Proportion
BA	2925-2926-2930	389 (57.4)	4	16.6
GO	5201-5206-5212	210 (31)	16	66.7
MG	3126-3129	31 (4.6)	1	4.2
TO	1714-1715	14 (2.1)	1	4.2
Northeast Region	PB, CE, PE, RN, AL	18 (2.7)	-	-
Southeast Region	PR, RS	2 (0.3)	2	8.3
Other states	MS, MT, PA	6 (0.9)	-	-
Bolivia	Santa Cruz	1 (0.1)	-	-
No information	-	7 (1)	-	-
Total	-	678 (100)	24	100

a: Brazilian states (IBGE 2014): Alagoas (AL), Bahia (BA), Ceará (CE), Mato Grosso (MT), Mato Grosso do Sul (MS), Minas Gerais (MG), Pará (PA), Paraíba (PB), Paraná (PR), Pernambuco (PE), Rio Grande do Norte (RN), Rio Grande do Sul (RS), Tocantins (TO).

than 10 children infected. Studies with less than 200 infected mothers could have a strong bias in relation to the rate of congenital transmission. Large studies were performed in only three countries (Argentina, Bolivia and Paraguay) and results from over 2,500 infected mothers gave a precise figure for the rate of transmission, which was remarkably similar between studies at 4-6% (Carlier & Truyens 2010, Howard et al. 2014).

In Brazil, studies are shorter and rates lower (Martins-Melo et al. 2014), begging the question: why? One reason is that the prevalence of congenital transmission in the last decade in Brazil is less than 1%, so it was necessary to study 10,000 pregnant women to obtain 100 infected women and a few cases of congenital transmission. However, even in the few reports where more than 100 infected mothers were studied, the prevalence of congenital transmission was lower than in the three countries referred to above.

An opportunity to unravel this mystery arose from a study performed by our group for other purposes. A national serological survey was conducted between 2002-2008 by collecting 104,954 samples on filter paper from children born after insecticides were sprayed throughout the country (Luquetti et al. 2011). Roughly one in every three municipalities in all of Brazil (with the exception of RJ) was included. We found 20 cases in which samples from the children positive for *T. cruzi* correlated with the positivity of the mothers. This confirmation was performed by blood collection from the child and the mother, using the same methodology as in this report (4 serological tests). These cases were labelled as congenital because vectorial and other mechanisms of transmission were ruled out. The striking and unexpected finding was that the majority (12) of these cases were found in a single state, RS. In this state, only 4,529 samples of filter paper were collected, as opposed to all the other states that contributed with 100,425 samples (i.e., at BA 16,489 samples were collected, with a single congenital transmission). In all the other states combined, only eight cases of congenital transmission were observed. This makes the rate of transmission in the rest of Brazil.

Geographical differences in Chagas disease clinical manifestations are well known and recognised (Prata 1975). Megaesophagus is prevalent mainly in central Brazil (de Rezende & Luquetti 1994). Mortality due to Chagas disease is higher in central Brazil, mainly GO and Minas Gerais. Specific treatment with nifurtimox (NFX) is less effective in Brazil than in other countries such as Chile and Argentina, however Prata et al. (1975) found a good response to the drug in RS. Cases of cardiopathy are recognised as infrequent in RS and cases of megaesophagus are mainly of group I, the less severe type (de Rezende & Luquetti 1994). These features are similar for the countries bordering RS, Argentina and Uruguay. All of this evidence indicates a similarity of the disease patterns between RS and other countries and calls attention to potential differences in the host or the parasite within Brazil.

Recently, *T. cruzi* has been recognised to be divided into six different groups called discrete typing units (DTUs), from TcI to TcVI (Zingales et al. 2009). They belong to different ecotopes and have a geographical distribution as follows.

Tc I has mainly been found in humans at the north of the Amazonian River. This type of *T. cruzi* has also been found in vectors and occasionally in humans below the Amazonian River. Very few autochthonous cases of congenital infection from Colombia, Venezuela, Central America and Mexico have been described. Cases found in the USA were all imported from mothers born in South America. The related cases found in Europe (Spain, Switzerland) were all from mothers born mainly in Bolivia.

TcII has been found in humans mainly in central Brazil, associated with megaesophagus and severe cardiopathy. We published a 1986 paper in which all chronic phase patients harboured TcII, at the time known as zimodeme 2 (Luquetti et al. 1986). From recent isolations from our chronic patients with haemoculture, it has been determined that TcII had a higher prevalence (unpublished observations).

Tc III and IV are infrequent, found mainly in mammals in the sylvatic cycle in the Amazonian Region. Few cases have been described in humans, mainly in Venezuela. No cases of congenital transmission have yet been reported.

TcV is the main DTU found in humans to the south of the Amazonian River in Chile, Bolivia, Argentina, Paraguay, Uruguay and the south of Brazil (Corrales et al. 2009). All these countries report large numbers of cases and neonatal transmission has been higher, with prevalence values approximately 4% and 6%.

TcVI has also been found in regions where TcV is present, but mainly in mammals and only occasionally in humans. A few reports of congenital transmission of TcVI have been reported thus far.

For the reasons outlined above, it is reasonable to propose that in central Brazil, where TcII is the main DTU isolated, this parasite subtype is responsible for the observed geographical differences in disease pattern, as evidenced by the high prevalence of megaesophagus and decreased efficacy of NFX in treated patients. Based on the results found in the current study, we suggest that TcII is also responsible for a lower rate of congenital transmission. These data are concordant with those found in the national survey and provide new evidence that the parasite subtype is an essential factor.

We conclude that in central Brazil, a region of TcII prevalence, congenital transmission is lower than in other countries of the South Cone and in other areas in the south of Brazil where TcV predominates. A relationship among TcII and lower congenital transmission is suggested. This is the first description of an association between a particular DTU (TcII) and the frequency of congenital transmission.

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