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Perinatal Screening for Chagas Disease in Southern Texas

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Abstract

Perinatal screening for *Trypanosoma cruzi* in a cohort of 4000 predominantly Hispanic women in southern Texas revealed that Chagas disease occurs with sufficient frequency (0.25%) that targeted perinatal screening should be considered to identify infected mothers and infants at risk for congenital infection.

Keywords

Chagas disease; congenital infection; newborn infant; *Trypanosoma cruzi*

An estimated 300 000 Latin American immigrants in the United States are infected with *Trypanosoma cruzi*, the parasite causing Chagas disease [1]. The southern states, including Texas, have established enzootic cycles of *T cruzi* and rare cases of autochthonous transmission have been documented [2–3]. The triatomine insect vector was identified in 97 of the 254 counties in Texas and *T cruzi*-infected vectors in 48 counties [4]. Implementation of blood donor screening for *T cruzi* has increased awareness of Chagas disease as an unmet medical need [5]. Between January 1, 2007 and January 3, 2013, 1750 blood donors, including more than 100 in Texas, had confirmed *T cruzi* infection [6].

Estimates of congenital transmission rates range from 1% to 10% [7]. Based on the number of births to Latin American-born women, *T cruzi* prevalence in their home countries, and a conservative estimate of 1%–5% vertical transmission, an estimated 63–315 infected infants are born each year in the United States [1, 8]. Most congenitally infected infants have mild or nonspecific findings at birth, and laboratory testing is required to identify them [9]. Severe disease occurs, but even these infants can have delayed detection [10, 11]. Congenital infection can be diagnosed in early infancy by molecular techniques or by visualizing *T cruzi* in cord or infant peripheral blood, and it can be detected in later

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infancy by serologic testing (after passively acquired maternal antibodies have decayed). Our objective was to determine *T cruzi* infection prevalence among women, many of whom were immigrants from Chagas-endemic regions, giving birth at Ben Taub General Hospital (BTGH) in Houston, TX. We also instituted follow-up of infants born to women with confirmed infection.

METHODS

Study Population

Specimens of placental cord blood were collected from consecutive deliveries at BTGH between March 2011 and April 2012. If cord blood was not available, residual maternal plasma was obtained. The study was approved by the Institutional Review Boards for Human Research at the Baylor College of Medicine and the Harris County Hospital District. Data on maternal age, ethnicity, gestation at delivery, and birthplace were collected from hospital records. Mothers with confirmed *T cruzi* infection were referred to the BTGH Tropical Medicine Clinic. Infants of infected mothers were evaluated at Texas Children's Hospital.

Laboratory Assays

Specimens were shipped frozen to the Centers for Disease Control and Prevention (CDC). Samples were tested by the Chagatest recombinante, v3.0 enzyme-linked immunosorbent assay (ELISA) (Wiener Laboratories, Rosario, Argentina) [3]. The ELISA cutoff was set at 0.300 optical density units above the mean absorbance of 3 negative control specimens. Specimens within the range of the cutoff ±10% were considered indeterminate and were rerun. The positive predictive value of the Chagatest ELISA is low because of the low prevalence of the infection in this population. In addition, no single assay is sufficiently sensitive and specific to be relied upon for the diagnosis of Chagas disease [1]. Chagatest ELISA-positive and indeterminate samples were tested by trypomastigote-secreted-excreted-antigen-immunoblot (TESA-IB) and immunofluorescent antibody assay (IFA). Reactivity to *T cruzi*-specific transsialidase antigens at 150–160 kDa was considered a positive result [12]. An IFA titer 1:32 or higher was considered positive. Consensus-positive samples were those with at least 2 positive tests [3]. Serum from longitudinally evaluated infants of infected women was evaluated by Chagatest ELISA and IFA. Infants 3 months of age or younger had a wet mount and *T cruzi* polymerase chain reaction (PCR) performed at CDC on peripheral blood specimens.

Data Analysis

Dichotomous outcomes were compared with the χ^2 test. Maternal age distribution was compared using a 2-tailed unpaired *t* test.

RESULTS

Of 4016 consecutive deliveries, 4000 had cord blood (3001) or maternal plasma (899) available for testing. The median maternal age of these 4000 women was 28 years (range, 13–46) and 85% were Hispanic. More than 75% were born in Latin America, most in

Mexico (50.2%), El Salvador (11.3%), Honduras (9%), or Guatemala (6.4%). Twelve percent were born in the United States (77.7% in Texas). The remaining women cited 81 other countries of birth; Nigeria (18.6%), Pakistan (7%), and Vietnam (6.8%) were the most frequent.

Twenty-eight of the women's blood samples (0.7%) were positive by Chagatest ELISA. Ten women were confirmed as infected by TESA-IB (3 women) or both TESA-IB and IFA (7 women). Infected women delivered live-born infants at term (8) or preterm (25 and 36 weeks) gestation (2 women). The 10 women consensus seropositive for *T cruzi* infection (0.25% of the cohort) were significantly older ($P = .007$) and significantly more likely to have been born in El Salvador ($P < .001$) than were seronegative women (Table 1). The women had a median of 4 (range, 1–6) prior pregnancies and 3 (range, 1–6) other living children.

Eight of the 10 infected mothers were interviewed. None had heard of Chagas disease and none reported family members with the diagnosis. None had been diagnosed with heart disease or told she had a heart arrhythmia; 1 had a 1-year-long history of constipation. All had lived in rural areas of Mexico or Central America; 6 lived as children in a mud or adobe home, some with palm-thatched roofs. The mother of 1 infant failed to keep several appointments but described her infant as healthy. Contact information was not current for 1 mother.

Six infants were initially evaluated at 2–3 months of age. Five term infants were healthy and had no findings, such as lymphadenopathy or hepatosplenomegaly, suggestive of congenital Chagas disease. The 25-week preterm infant required supplemental oxygen but otherwise was thriving. Testing was negative by PCR and wet mount for these 6 infants. Two of these 6 had a positive Chagatest ELISA or IFA, but, at 5–6 months of age, serology was negative. Two additional infants, first evaluated at 7 months of age, were seronegative.

DISCUSSION

Our finding of a confirmed *T cruzi* infection prevalence of 0.25% is lower than the estimates of 1% for Mexico and 3.1%–3.4% for Central America [1]. Prevalence increases with age in the general population in endemic countries, so the younger age of pregnant women may account for this difference. Nevertheless, our findings suggest that a substantial number of *T cruzi*-infected women give birth in the United States each year, and they provide direct data to begin to assess the Chagas disease burden in Texas and other states with large numbers of Latin American-born residents [13]. Because of the small number of infected mothers and the 1%–5% estimated transmission risk, it is not surprising that we found no infected infants.

Detection of maternal infection is important for the woman herself, for her infant, and for her other children, who may also have been infected congenitally [14]. Most of the infected women we identified had had multiple prior pregnancies. Identification of an infected woman should trigger testing of the infant as well as any older children. Early in life, the diagnosis of congenital Chagas disease is established by visualizing *T cruzi* in

cord or infant peripheral blood and/or by use of molecular methods [8]. Molecular and parasitological testing in a single specimen has only 40%–75% sensitivity for congenital infection; repeated testing is often necessary to rule out infection [7, 8]. Results of serologic testing, as with our cohort of infants, should be negative by 9 months, when passively acquired maternal antibodies are no longer present. Treatment of congenital infection is well tolerated and highly effective with rates of cure that exceed 90% when antitrypanosomal drugs are instituted early in life [11]. The mothers are at risk for later manifestations of chronic *T cruzi* infection, including progressive cardiac disease, and a thorough evaluation is indicated, followed by consideration of antitrypanosomal drug treatment after breastfeeding ends [14].

The first reported case of congenital transmission of Chagas disease in the United States was confirmed recently by CDC [11]. The presentation in this preterm infant with fetal hydrops, ascites, pleural effusion, and pericardial effusions highlights the potential severity and yet nonspecificity of *T cruzi* infection in infancy. Clinical findings can include prematurity, hepatosplenomegaly, jaundice, anemia, and thrombocytopenia [10, 15]. However, even life-threatening manifestations of congenital infection, such as anasarca, pneumonitis, and meningoencephalitis, are not specific to Chagas disease, and a high index of suspicion is required to establish the diagnosis [15]. Most congenitally infected infants appear healthy, but they are at risk to develop life-threatening cardiac or gastrointestinal disease decades later.

It is difficult to know whether targeted screening for Chagas disease should be implemented. Congenital infection with *T cruzi* has similarities to congenital toxoplasmosis for which screening is conducted in several states. Both are low-incidence infections that often are asymptomatic at birth and can have serious sequelae later in life if unrecognized [16]. There is potential benefit to the mother from screening for Chagas disease because her infection is identified and possibly to her exposed infant and any other children, if congenital transmission has occurred. The estimated incidence of congenital *T cruzi* infections (63 to 315 per year) falls within that of the 29 core conditions included in the American College of Genetics uniform screening panel, between the 6th (medium-chain acyl-coenzyme A dehydrogenase deficiency with 239 annual births) and the 14th (partial and complete biotinidase deficiency with 62 births) most frequent disorders detected [17].

The availability of effective treatment to prevent the potentially life-threatening consequences of Chagas disease in later life raises the importance of detecting infected infants early in life, when treatment is best tolerated and most effective. Current screening requires multiple steps, from maternal serology to several assays in infants, and is a challenge to mount on a large scale, although use of this type of program has been demonstrated in Chagas-endemic countries [18]. Development of a sensitive antigen or DNA detection assay for cord or newborn blood would potentially allow Chagas disease testing to be incorporated into targeted newborn screening programs in states with high numbers of at-risk immigrants. Nevertheless, our findings demonstrate that it is feasible to screen for Chagas disease in an at-risk population and to evaluate the infants of infected women for congenital Chagas disease.

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Table 1.

Demographic Features of 4000 Delivering Pregnant Women Tested for Chagas Disease

	Trypanosoma cruzi Serologic Status[a]		
Maternal feature	**Positive (n = 10)**	**Negative (n = 3990)**	***P* Value**
Mean years of age (range)	33.8 (25–41)	28.3 (13–46)	.007
Hispanic ethnicity	10 (100)[b]	3376 (84.6)	NS
Birthplace			
Mexico	3 (30)	2001[c] (50.2)	NS
El Salvador	5 (50)	447 (11.2)	<.001
Honduras	2 (20)	357 (8.9)	NS
Guatemala	0	258 (6.5)	NS
Nicaragua	0	17 (0.4)	NS
Live birth (%)	10 (100)	3880 (97.2)	NS

Abbreviations: ELISA, enzyme-linked immunosorbent assay; IFA, immunofluorescent antibody assay; NS, not significant; TESA-IB, trypomastigote-secreted-excreted-antigen-immunoblot.

[a] Based on positive results on at least 2 of 3 serological assays (Chagatest ELISA, TESA-IB, IFA);

[b] Percent.

[c] Numbers represent the seronegative women born in each country.