

# Control of mother-to-child transmission of Chagas disease: the Tuscany Region model

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**Abstract:** Chagas disease is an endemic parasitosis in Latin America where the main route of transmission is vectorial. In Europe, due to migration phenomena, Chagas disease cases are increasing and the main way of transmission is mother-to-child, perpetuating the infection from one generation to the other. Congenital Chagas disease is in most cases asymptomatic at birth, but, if not diagnosed and treated early, it puts the child at risk of developing severe cardiac and gastrointestinal problems throughout life. According to the Regional Resolution throughout the territory of Tuscany, pregnant women born in continental Latin America (or born to a mother born in that area) should be offered free of charge serological test for Chagas disease during pregnancy or at delivery, with the main objective of controlling and stopping the transmission of the disease.

**Keywords:** Chagas disease, Pregnancy, Screening, Latin America, Neglected Tropical Diseases

## Introduction

Chagas disease is a parasitic disease caused by the protozoan *Trypanosoma cruzi*; it is endemic in continental Latin America, where it is mainly transmitted by blood-sucking triatomines (vectorial transmission). Twenty-one countries are endemic for Chagas disease: Argentina, Belize, Bolivia, Brazil, Chile, Colombia, Costa Rica, Ecuador, El Salvador, Guatemala, Guyana, French Guiana, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Suriname, Uruguay, Venezuela<sup>1</sup>. The disease, which in the endemic area is often acquired in pediatric age, is characterized by an initial acute phase, generally oligosymptomatic, which remains unrecognized in the majority of cases. The infected subject subsequently enters the chronic phase of the disease, which in most cases (~70%) remains asymptomatic for life. However, about 30% of infected individuals, after a latency of several years (usually 20 to 30 years), develop severe heart involvement (arrhythmias, cardiomegaly, congestive heart failure, sudden cardiac death) or gastrointestinal complications (megaesophagus, megacolon)<sup>2</sup>.

Chronically infected individuals, often unaware of their condition, can transmit the disease through blood transfusions, organ transplants and, and in case of pregnant women, to their child. The risk of maternal-fetal transmission during pregnancy is around 3% to 5% and the infection of the newborn child is referred to as congenital Chagas disease<sup>3</sup>. Congenital Chagas disease is asymptomatic at birth in the majority of cases (60-90%), with the possibility for the child to later develop the chronic complications of the disease as above mentioned. In a minority of cases (about 10%), signs and symptoms of a severe systemic infection may be present at birth: prematurity, low birth weight, hepatomegaly, splenomegaly, anemia, ARDS, anasarca, myocarditis, meningoencephalitis are

the most common complications of congenital Chagas disease<sup>4,5</sup>.

## Chagas disease in non-endemic areas

In continental Latin America, Chagas disease represents a major public health problem, affecting 6-8 million people today. Due to the significant increase in migratory flows from Latin America to the more industrialized countries and the possibility of non-vector transmission, Chagas disease is now an emerging health problem in numerous non-endemic areas, including Italy<sup>6</sup>. Italy is indeed the second country in Europe and third in the world (after the United States and Spain) for the number of migrants welcomed from Latin America. In 2020, according to the Istituto Nazionale di Statistica (ISTAT) data, there were 366,343 Latin American migrants in Italy, of which 223,260 (60.9%) were women<sup>7</sup>. Using the estimated seroprevalence in the countries of origin, it can be hypothesized that between 4,700 and 9,700 people are affected by Chagas disease in Italy, of which 2,900-5,900 are women<sup>8-11</sup>. Based on seroprevalence data in endemic countries, epidemiological data in our country and estimated congenital transmission rate of the disease, it was estimated that between 2014 and 2018, 463 (95% CI 267-792) women with Chagas disease gave birth and 16 (95% CI 12-21) newborns could have been born with congenital Chagas disease; however, only three newborns were actually diagnosed in the same period<sup>12</sup>. Similar data were reported in the Spain, where a 60% rate of underdiagnosis among children younger than 14 years old was estimated<sup>13</sup>.

The main factors influencing these data are lack of awareness and of knowledge of the disease among health care workers, worsened by the perception that Chagas disease is a very rare pathology in our latitudes, therefore not having a big epidemiological impact<sup>14,15</sup>. However, lack of diagnosis could rather reflect

the absence of screening programs, which need to be implemented in order to uncover the real burden of this pathology<sup>16</sup>.

With the described epidemiological scenarios, in 2009 the World Health Organization, in collaboration with some delegates from European countries, has drawn up an official document that highlights the emerging problem of Chagas disease in Europe and recommends local health authorities to implement adequate measures for control and prevention<sup>17</sup>.

However, while programs aimed to control the transmission of Chagas disease through blood transfusions and organ transplants are widely implemented in Europe and in Italy at national level, programs aimed to control of mother-to-child transmission of the disease are lacking throughout Europe<sup>17,18</sup>.

There are only a few, localized examples of pioneer screening programs for control of congenital Chagas disease in Europe, such as those implemented in Valencia, Galicia and Catalonia, in Spain, where health policies have been adopted to control the congenital transmission of the disease<sup>19-21</sup>.

At the moment, in Italy, national policies aimed to the control of mother-to-child transmission of Chagas disease do not exist. In this perspective, it is worth of note that much rarer pathologies, such as phenylketonuria and cystic fibrosis, are included since 1992 in the "extended neonatal screening" which is provided by the Italian law<sup>12</sup>.

However, the first screening programs offering serological tests to Latin American pregnant women have been introduced in some realities, such as the province of Bergamo<sup>22</sup> and the Tuscany Region, which represents, together with those in Spain, one of the very few contexts in Europe where health policies have been implemented for the control of congenital transmission of the disease.

#### **The Tuscany Region model for congenital Chagas disease control**

With three regional resolutions, approved respectively in 2012, 2015 and 2019, the Tuscany Region has indeed included, among the free tests to be performed during pregnancy, the serological test for Chagas disease screening for women who were born in continental Latin America or who were born to a mother from that area. The laboratory test should be performed in the first trimester of pregnancy, when the pregnant woman is first taken in charge by obstetricians and gynecologists, but if this does

not happen, it can still be performed later at any time during the pregnancy or during delivery. The test involves a simple venous blood sample on which a serological test is performed to search for IgG antibodies against *T. cruzi*<sup>23</sup>.

Women who test positive are addressed to the Tuscany Referral Center for Tropical Diseases, where further investigations are conducted to establish the stage of the disease and the presence of any late complication of Chagas disease. After the end of breastfeeding, affected women are eventually offered antiparasitic treatment. The treatment, based on benznidazole, is in fact contraindicated in pregnancy and during breastfeeding<sup>2</sup>. The finding of maternal infection will allow the evaluation of the newborn through parasitological, biomolecular and serological tests; in case of documented congenital infection, the newborn will be treated with antiparasitic treatment, which is estimated to be 100% effective if it started in the first year of the child's life, while effectiveness tends to decrease progressively if the chronic phase of the disease is prolonged<sup>24</sup>.

From a preliminary evaluation of the data collected at Careggi University Hospital, where a pilot project had already started in 2008, it appears that since 2012 the Tuscany regional program has reached about 45-50% of pregnancies at risk. Screening coverage is therefore estimated to be even lower among the other hospitals throughout the Tuscany Region. These data evidence the need to widely promote the knowledge of the "Program for the prevention and control of congenital Chagas disease in Tuscany Region" to all professionals involved, through awareness raising and training events aimed at midwives, nurses, general practitioners, gynecologists, neonatologists, pediatricians and health assistants.

In this perspective, since 2019, a training course entitled "Chagas in pregnancy: the program in Tuscany Region", aimed to all health care providers in the Region, was held at Careggi University Hospital. The course is intended to increase awareness towards Chagas disease, describing the main features of the pathology, with a focus on congenital transmission and illustrating the main points of the regional protocol. An online version of the course has been offered and is still available<sup>25</sup>.

Moreover, in 2019 the so called "Chagas checklist" was introduced within the clinical informatic system in Careggi University Hospital, with the

aim of making it easier and more automatic for the health care provider to remember that Chagas disease screening test is recommended if the pregnant woman is at risk.

### Conclusion

In conclusion, we believe that programs such as the one implemented in the Tuscany Region are fundamental for monitoring screening coverage in women at risk and to promote systematical screening in people at risk, representing the best strategy to control transmission of Chagas disease from mothers to their children.

We also support the use of informatic tools such as the “Chagas check-list”, together with online and onsite training courses, which have an important role for the success of these kind of programs.

Moreover, it has been demonstrated that Chagas disease screening programs are strongly cost effective, not only when screening is addressed to pregnant women and the newborns, but also when the adult population is involved, if costs are compared with those of diagnosing, managing and treating the late complications of the disease<sup>26,27</sup>. The detection of a *T. cruzi* seropositivity will also permit to extend the screening to other family members or subjects coming from or still living in the same town or community.

Lack of sensitivity and awareness towards the disease can partly explain the still too low screening coverage in Tuscany Region; another big limitation is that the Chagas disease screening test, even offered for free to women at risk, is not included in the official pamphlet where all the exams to be done during pregnancy are prescribed as provided by the Italian law, needing to be prescribed on a separate prescription.

Another point of weakness is that this project was funded only for what concerns the cost of the screening tests and of the clinical management and follow-up of positive women and their children, while promotional, educational and training activities were not covered.

Sharing the example of the model implemented in Tuscany Region, we aim to encourage the implementation of congenital Chagas disease screening programs in many other settings in non-endemic countries, which are needed at national and European level, and to underline the need of higher attention towards this growing health issue among health care workers and health policies makers.

We believe that better knowledge and awareness

of this burden among all health care workers, including nurses, health assistants, obstetricians, general practitioner and all physicians and not only infectious diseases specialists, are key elements for the control of congenital Chagas disease; only through homogeneously spread and solidly implemented national programs, the burden of congenital Chagas disease could be controlled and its perpetuation from one generation to the other could be interrupted.

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