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Congenital Chagas disease in a non-endemic area: Results from a control programme in Bergamo province, Northern Italy

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ABSTRACT

Introduction: In non-endemic countries, one of the most important routes of transmission of *Trypanosoma cruzi* is vertical transmission. The objective of this work is to report the results of the screening activities for the control of congenital Chagas Disease (CD) implemented in Bergamo province between January 2014 and December 2016.

Methods: The programme addressed Bolivian pregnant women settled in Bergamo province. All the eight hospitals offering antenatal and delivery care in that area were involved. We retrospectively calculated the coverage rate of the screening programme, the prevalence of CD in this population, as well as transmission rate to their offspring.

Results: During the study period, 376 Bolivian women accounted for 387 deliveries. The coverage rate of serologic screening was 85.6%. Confirmed seropositive women were 28, accounting for a prevalence of CD of 8.7% (95% IC 5.9–11.5). Among 29 children born to positive mothers, one infected child was detected (transmission rate of 4.3%, 95% IC 0–12.6) and treated accordingly. Other 13 children previously born from the same mothers were retrieved and tested for CD: no additional congenital cases were diagnosed.

Discussion: Our screening programme presented a high coverage, although widely variable in the different birthing facilities. National guidelines recommending CD testing in pregnant women would help to increase case detection countrywide.

1. Introduction

In Europe, Spain is the largest recipient of migrants from Latin American (LA) countries, followed by Italy. Accordingly, the estimated number of people affected by Chagas disease (CD) in Europe is highest in these two countries. In particular, the prevalence of CD among LA migrants present in Italy has been estimated from 3.9% [1] to 4.2% [2], with the highest figure in Bolivians (18%) [2]. In non-endemic countries, one of the most important routes of transmission of *Trypanosoma cruzi* is vertical transmission, so that the World Health Assembly, with the resolution WHA63.20 in 2010, urged actions to tackle the problem. Although recent studies demonstrated that the screening for CD is cost-effective [3,4], a national health policy regarding its control is still

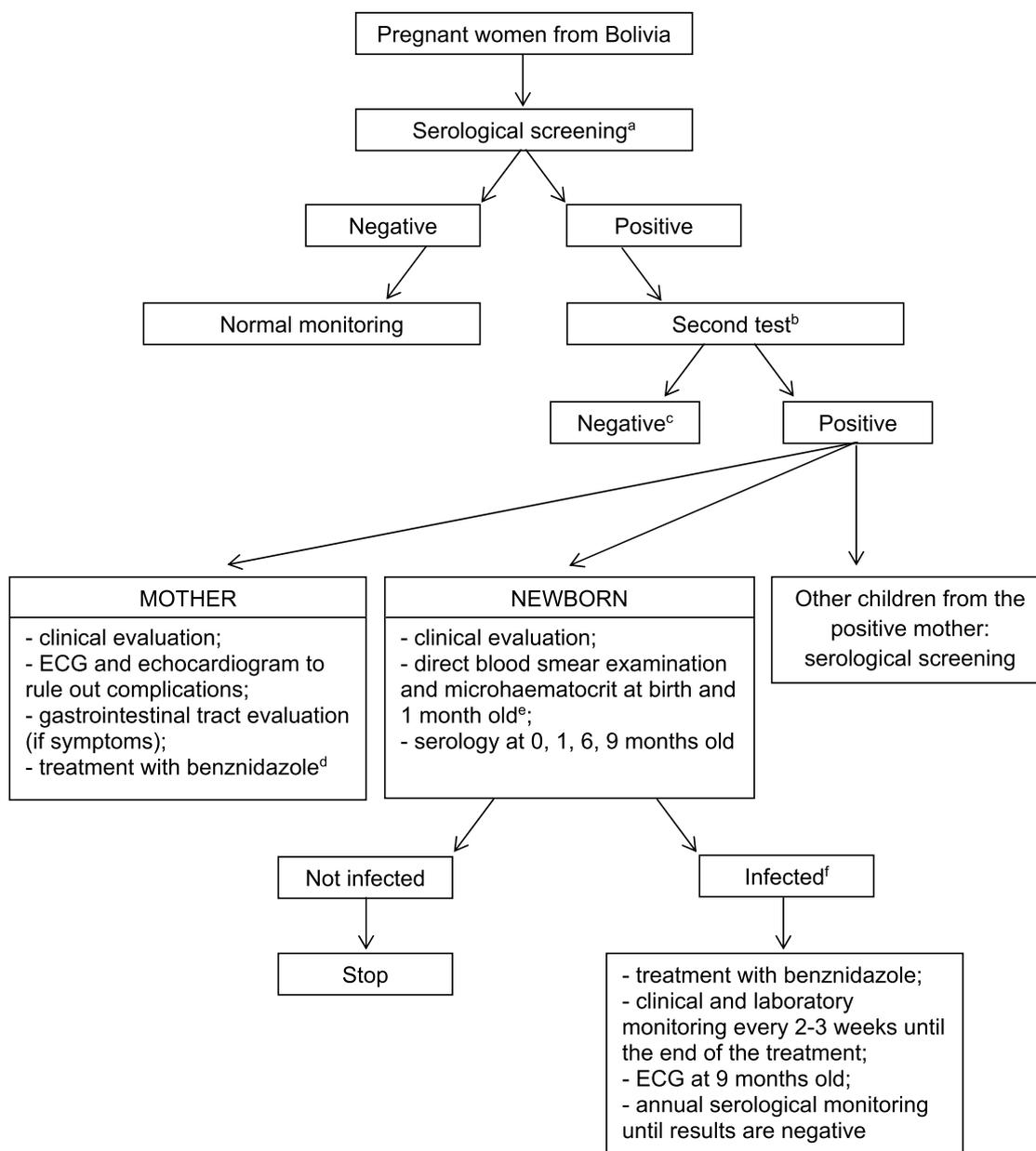
lacking in Italy. A few local initiatives targeting this issue have been implemented: Tuscany region has started a congenital CD (cCD) control programme in 2012, followed by Bergamo province in 2013. Moreover, cCD surveillance programmes are also underway in single centres in Negrar (Verona), Rome and Bologna [5,6].

According to official data [ISTAT 2016, <https://www.istat.it/it/lombardia>, accessed on 03/06/2017], Bergamo province, one of the largest provinces in the Lombardy region, Northern Italy, has a population of around 1.1 million inhabitants, including about 125.500 migrants [<http://www.asr-lombardia.it/ASP-Bergamo/popolazione/stranieri/lombardia-e-province/tavole/7578>, accessed on 03/06/2017]. Among them, Bolivians are 6.068 (around 10.000 if undocumented people are considered), representing 42.6% of all Bolivians

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^a ChLIA (ABBOTT PRISM Chagas) - sensitivity 100% and specificity 99%.

^b CMIA (ABBOTT ARCHITECT Chagas) - sensitivity 100% and specificity 99.5%.

^c In case of discordant tests, serology is repeated one month apart.

^d Benznidazole administration is not recommended during pregnancy and breastfeeding.

^e Real-time Polymerase chain reaction (PCR) is not routinely available, but it can be performed at Istituto Superiore di Sanità - ISS (Rome) if necessary.

^f Parasitological diagnosis or still positive to serologic test at the age of 9 months.

Fig. 1. Flowchart for screening and management of Bolivian pregnant women and their newborns.

resident in Italy. The first phase of the screening programme implemented in Bergamo province addressed Bolivian pregnant women, in order to ensure early diagnosis and treatment of cCD cases, as well as to guarantee treatment to mothers and reduce the risk of transmission of CD in case of further pregnancies.

The aim of this work is to report the results of the screening

activities conducted in Bergamo province between January 2014 and December 2016.

2. Methods

All the eight hospitals offering antenatal and delivery care in

Bergamo province were involved. The project included meetings with healthcare professionals (including gynaecologists, obstetricians and paediatricians) to inform about the importance of performing serology for CD in Bolivian pregnant women, in addition to TORCH (toxoplasmosis, rubella, cytomegalovirus, herpes simplex, HIV) screening. Papa Giovanni XXIII Hospital was the referral centre for diagnosis and treatment of all adult and paediatric CD cases.

The programme flow is summarized in Fig. 1. A chemiluminescent immunoassay (ChLIA, ABBOTT PRISM Chagas) was used for the first screening, and, in case of positive result, the test was repeated using a more specific technique (chemiluminescent microparticle immunoassay, CMLA, ABBOTT ARCHITECT Chagas).

Infants born to CD affected mothers were monitored through their first nine months of life. The protocol established the use of parasitological tests (direct blood smear examination and microhaematocrit) at birth and 1 month old, together with serological monitoring. Real-time PCR (*T. cruzi* genesig[®] Advanced Kit, PrimerDesign™, UK) for *Trypanosoma cruzi* is not routinely available yet, but it can be performed at Istituto Superiore di Sanità (ISS, Rome) in selected cases. Children who did not present to the scheduled visits were declared lost to follow up, after at least two recall attempts.

The coverage rate was calculated as the proportion of women tested on the total number of Bolivian women who delivered in any hospitals included in the programme. The prevalence of CD was defined as the proportion of confirmed seropositive women over the number of tested women. Finally, transmission rate was calculated as the proportion of infected children on the total number of children born to positive mothers. Data analysis was performed using Epi-Info 7, 2015.

3. Results

During the 3-year period, 376 Bolivian women accounted for 387 deliveries. Their mean age was 31.3 ± 5.9 years (range, 16–44). Overall, the coverage rate of serologic screening was 85.6% (322/376), but relevant disparities were found among the hospitals involved (Table 1).

Confirmed seropositive women were 28, accounting for a prevalence of CD of 8.7% (95% IC 5.9–11.5).

Twenty-nine children were born to positive mothers, including one pair of twins. The adherence rate to follow-up was 88.5%, since 3 children were lost. Three children are currently under monitoring (hence excluded from the calculation of transmission rate), 22 children resulted negative to the screening, and one infected child was detected, accounting for a transmission rate of 4.3% (1/23, 95% IC 0–12.6). The child was a preterm baby, born at 34.4 weeks to a 31-year-old woman with indeterminate CD. Parasitological tests were negative both, at birth and 1 month old. At a later time, the infant developed haemolytic anaemia, requiring blood transfusion. Since parasitological tests were previously negative, real-time PCR for *T. cruzi* was required, with a positive result. Meanwhile, other possible causes of anaemia were excluded. Treatment with benznidazole at increasing dosage (up to 10 mg/kg) was administered for 2 months, with excellent tolerability.

Table 1

Distribution of deliveries of Bolivian women and screening coverage by hospital in Bergamo province.

Hospital	Number of deliveries (2014–2016)	Pregnant women tested	Coverage %	Positive (%)
Papa Giovanni XXIII - Bergamo	238	222	96.9	24 (10.8)
Eastern area	84	66	80.5	2 (3.0)
North-Eastern area	41	29	70.7	1 (3.4)
Western area	10	3	30.0	1 (33.3)
North-Eastern area	6	0	0	0 (0)
South-Eastern area	4	1	25.0	0 (0)
South-Western area	3	1	33.3	0 (0)
Northern Bergamo	1	0	0	0 (0)
Total	387	322	85.6	28 (8.7)

Anaemia resolved and PCR for *T. cruzi* became negative. The child was monitored over 15 months, when serology resulted negative. In another asymptomatic newborn, serology persisted positive at the age of 9 months, but with decreasing titre compared to previous tests. In this case a “wait and see” strategy was adopted: a further serologic test performed at 12 months resulted negative, ruling out cCD.

Furthermore, other 13 children previously born to the CD-positive mothers were retrieved and tested for CD: no additional congenital cases were diagnosed.

4. Discussion

Globally, our screening programme presented a high coverage, although widely variable in the different birthing facilities. The highest coverage was recorded where the majority of deliveries were attended, primarily at the referral centre Papa Giovanni XXIII Hospital (96.9%). Moreover, 88.5% of children born from an affected mother completed the follow-up, a good result if compared with the Catalonian programme, which counted 79.8% children who completed the 9 month follow-up in 2011 [5]. However, a huge difference in the magnitude of the population screened separates the two interventions. Currently, in Italy other programmes are ongoing to control vertical CD transmission: at Regional level (Tuscany Region), and at single Institutions [7]. No data on the coverage of those programmes are available, so far. In non-endemic areas, Spain is hosting one of the biggest Latin American communities, and different programmes for the control of congenital Chagas disease have been implemented: in Valencia since 2009, in Catalunya since 2010, in Galicia since 2012, and in Madrid since 2013 [7]. Data on programme coverage are available for Valencia, where the 95.4% of the target population was tested [8], whereas in Catalonia from 2010 to 2011 the programme coverage passed from 65 to 85% [7].

The overall prevalence of CD among Bolivian pregnant women was 8.7% in our programme, lower than that previously reported in other studies in Spain [9–11], Switzerland [12] and also in Bergamo province among Bolivian adults [13]. This lower prevalence is probably related to the younger age of our population compared to that of other studies, the youngest being less exposed to the infection as a consequence of the advances obtained in vectorial control in endemic countries, including Bolivia.

A recent meta-analysis showed that congenital transmission of CD in endemic countries was higher than in non-endemic countries (5.0% versus 2.7%), although there is a high variability in the literature [14]. We found a transmission rate of 4.3%, which is close to that reported from endemic countries [15,16]. However, the small simple size of this study limits the interpretation of these results.

Another limitation should be recognized: at the beginning, the programme was focused only on Bolivian community. This choice was linked to several considerations. First of all, among LA people resident in Bergamo area, Bolivians are the most numerous, and generally more conscious of CD; other nationalities (mainly Peruvians and Ecuadoreans) are much less present. Moreover, before 2013, access to testing and treatment for CD was challenging in Bergamo [13], as

currently it is the case in the great part of Italy. Answering to this health need, the screening programme was implemented with limited resources within the services offered by the Regional Health System, which means with no charge for the users.

Nevertheless, our data confirm that a screening of pregnant women is feasible in non-endemic countries. Early diagnosis of cCD allowed starting treatment within the first year of life, and this approach guarantees a cure rate next to 100% [17]. Furthermore, screening gave the opportunity to increase case detection, offering the test not only to asymptomatic women, but also to their relatives.

Given that the cost-effectiveness of testing for CD has been demonstrated not only for pregnant women but also for asymptomatic adults [3], the programme was expanded since 2016 to all Latin Americans, regardless pregnancy status or country of origin.

At present, national guidelines recommending CD testing in LA people and particularly in pregnant women (in addition to the TORCH screening already ongoing) are still lacking: we believe that extending the access to testing and treatment could be a key public health intervention to control CD transmission countrywide.

Conflicts of interest

The authors declare no conflict of interest.

Author's contributions

PR and MR conceived and designed the study; PR, GG, LT, GB, MM, MR and SR contributed in the acquisition of data; PR and AA analyzed and interpreted the data; PR and AA drafted the manuscript; LS and MR revised it critically; all authors approved the final version of the manuscript.

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