Surveillance of Chagas disease in pregnant women in Madrid, Spain, from 2008 to 2010

M D Flores-Chavez[1], F J Merino[2], S García-Bujalance[3], P Martin-Rabadán[4], P Merino[5], I García-Bermejo[6], A Delgado[7], J Cuadros (jcuadros.hupa@salud.madrid.org)[8], Working Group on Chagas Disease of Autonomous Community of Madrid[9]

1. Department of Parasitology, National Microbiology Centre, Instituto de Salud Carlos III (Carlos III Health Institute), Madrid, Spain
2. Department of Microbiology and Parasitology, Hospital Universitario Severo Ochoa, Leganés, Madrid, Spain
3. Department of Microbiology and Parasitology, Hospital La Paz, Madrid, Spain
4. Department of Microbiology, Hospital Gregorio Marañón, Madrid, Spain
5. Department of Microbiology, Tropical Medicine Unit, Hospital Clínico de San Carlos, Madrid, Spain
6. Department of Microbiology, Hospital Universitario de Getafe, Madrid, Spain
7. Department of Microbiology, Hospital Universitario Fundación Alcorcón, Madrid, Spain
8. Department of Microbiology and Parasitology, Hospital Príncipe de Asturias, Madrid, Spain
9. The participants of this group are listed at the end of the article

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One of the most important modes of transmission of *Trypanosoma cruzi* infection in areas where it is not endemic is vertical transmission: from mother to child. The objective of this report is to assess the efficacy of different programmes of serological screening to monitor infection with *T. cruzi* in pregnant Latin American women living in Madrid (Spain). To achieve this, a retrospective study was undertaken from January 2008 to December 2010 in seven hospitals in the Autonomous Community of Madrid. Serological screening programmes were classified in two main strategies: a selective one (pregnant women from Bolivia) and a universal one (pregnant women from Latin America). A total of 3,839 pregnant women were tested and the overall prevalence was 3.96%. The rate of congenital transmission was 2.6%. The current monitoring programmes have variable coverage ranging between 26% (selective screening) and 100% (universal screening). Monitoring of pregnant women from Latin America only reaches full coverage if universal screening of pregnant women is carried out at any moment of pregnancy, including at delivery. A common national regulation is necessary in order to ensure homogenous implementation of screening.

Introduction

In the last ten years, due to the increase in the immigrant population from Latin America, *Trypanosoma cruzi* infection has become one of the most common imported parasitoses in Spain. By the end of 2009, around 3,600 cases had been confirmed, although estimates that take into account the prevalence of *T. cruzi* infection in Latin America suggest that between 40,000 and 65,000 affected people currently reside in Spain [1].

Taking into account the data provided by the Spanish Statistical Institute (INE) in January 2010, 25.7% (429,826 of 1,670,196) of the immigrant population from *T. cruzi*-endemic areas were residing in the Autonomous Community of Madrid (Figure). Of this population, 39.1% (167,917 of 429,826) were women aged between 15 and 44 years [2].

The three main transmission routes of *T. cruzi* in non-endemic regions are: transfusion of blood products, vertical transmission and organ transplantation [1]. That is why, between March 2002 and December 2004, the Madrid branch of the Spanish Red Cross carried out the first serological screening of candidates for blood donation from areas where Chagas disease is endemic, to establish their suitability as donors. The potential donors, who were not born in Spain, were interviewed and 44% of them were identified as coming from endemic areas. The prevalence of *T. cruzi* antibodies in the donors coming from endemic areas was 0.8% and 75% of those who tested positive were from Bolivia [3].

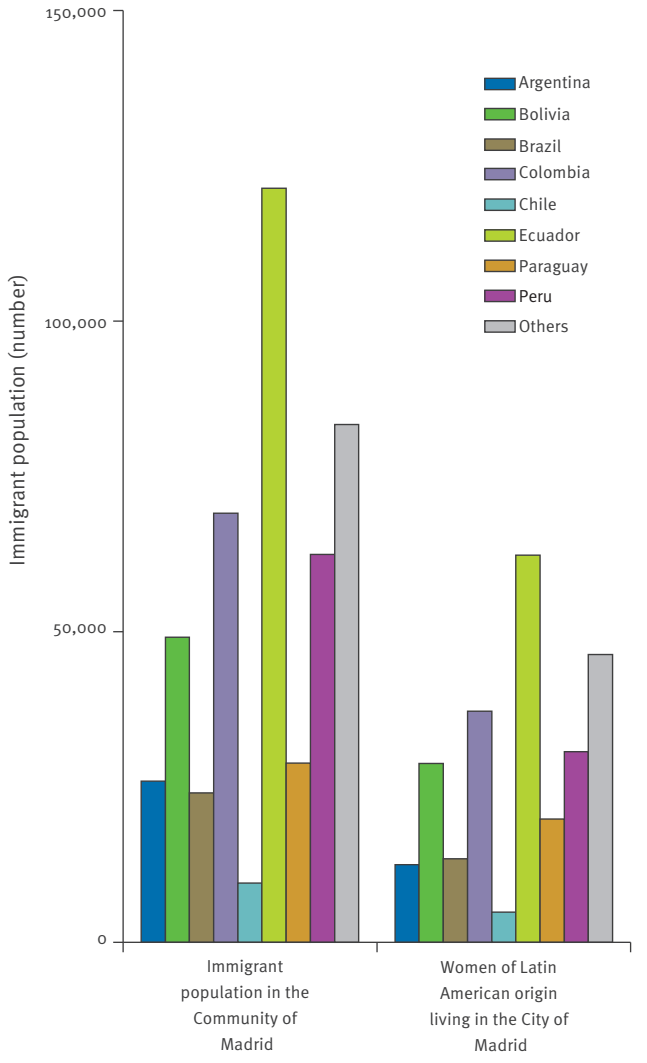
Since September 2005, in accordance with the Royal Decree RD1088/2005 [4], all blood transfusion centres in Spain have been obliged to carry out serological screening of the population considered to be at risk [4]. This means that they systematically exclude from donation individuals (i) who come from areas where Chagas disease is endemic, (ii) who were born to mothers from such areas, and (iii) who have received transfusions or have spent prolonged periods of time in such areas (one month or longer in mainly rural areas) [5,6]. In the past 22 years, there have been at least six cases of transfusional Chagas disease in Spain: one of them was reported in Madrid and proved fatal [7,8].

Another important mode of infection is vertical transmission from a seropositive mother to her child during pregnancy or delivery. At present, there is no national Spanish policy that establishes monitoring of Chagas disease in pregnant women and their newborns. Only the Autonomous Communities of Valencia and Catalonia have regulations in place and have systematically performed screening since November 2007 and February 2009, respectively [9,10]. Nevertheless, it is important to mention that there are different initiatives in other Communities. To date, cases of congenital infection have been reported in Valencia, Catalonia, Murcia, Aragon, the Basque Country and Andalusia [1].

In Madrid, as in other areas of Spain, the birth rate has increased among the migrant population in the last five years. In 2009, of the 35,038 deliveries registered in Spain to mothers from Latin America, 9,171 (26.2%) were to mothers resident in Madrid. The most common countries of origin of these mothers were: Ecuador, Colombia, Bolivia and Peru (27.9%; 12.9%; 12.7% and 11.7%) [2].

Figure

Immigrant population and women born in Latin America and registered in the Municipal Register of Madrid, Spain, January 2010



Source: Spanish Statistical Institute (www.ine.es).

Currently, the only way to control Chagas disease in pregnant women is determining the presence of *T. cruzi* antibodies in those who come from areas where the infection is endemic, thus facilitating early diagnosis and treatment of congenital infection and also allowing postnatal treatment of the mother to reduce the risk of transmission in future pregnancies. Therefore, the main objective of this report is to describe and assess different programmes to monitor pregnant women coming from different areas in Latin America, because treatment of children leads to a cure rate next to 100% whereas it is much lower in adults [11].

Material and methods

The serological screening of pregnant women at risk of *T. cruzi* infection was implemented within the framework of the Working Group on Chagas Disease of the Madrid Autonomous Community. This study assesses observationally and retrospectively the general coverage of the screening programme, the prevalence of infection and the rate of congenital transmission. The study included seven hospitals serving 48.5% (3,131,315 of 6,458,684) of the population of the Autonomous Community of Madrid, according to INE data in January 2010.

The programme included meetings to inform healthcare personnel and managers in the public hospitals involved and to draw attention to the need to incorporate a test to detect *T. cruzi* antibodies as an additional routine test performed on pregnant women from areas where Chagas disease is endemic.

Since there is no standard reference test, each hospital chose a serological test in accordance with its infrastructure. This determined the type of screening, which was either universal (applied to all pregnant women from countries where the disease is endemic - option 1; or to all pregnant women from Latin America - option 2) or selective (applied only to pregnant Bolivian women - option 1; or to pregnant Bolivian women plus pregnant women born in both low-risk and high-risk areas according to maps indicating distribution in particular countries or other risk indicators - option 2). For this last option, all pregnant Bolivian women were considered to be from a high-risk area, and the rest of Latin American pregnant women were considered to come from low-risk areas. The serological screening for Chagas of low-risk pregnant women was carried out taking into account the recommendations and maps for the selection of blood donors [5,6,12] and their clinical epidemiological background.

On the other hand, depending on the specific organisation of each hospital and the attendance of pregnant women at their prenatal sessions, serological screening was systematically performed only in the first or

second trimester, or at any moment of the pregnancy including delivery (Table 1).

For the detection of cases of congenital infection, an agreed follow-up protocol was used which involved monitoring children born to seropositive mothers during the first nine months of life [13]. Tests were performed at delivery, after one month, and at nine months of age, while the option of performing more tests during the first nine months was not ruled out. The parasite detection was carried out by direct microscopic observation, microhaematocrit test [15] and PCR [8].

Data were collected via a form designed for the analysis of aggregate data. The coverage of each screening programme was calculated as the proportion of pregnant women tested of the total number of pregnant women attending the seven hospitals from areas where the disease is endemic, from January 2008 to December 2010. The overall prevalence was calculated as the proportion of pregnant women confirmed as positive of the total number of pregnant women tested. Any pregnant woman born in Cuba, the Dominican Republic or any other country where Chagas disease is not endemic, was excluded from the analysis. The prevalence by country of origin was defined as the proportion of pregnant women confirmed as positive from each country of the total number of pregnant women tested from that country. For this last calculation, the data used were those from hospitals that recorded the country of origin of the entire population of pregnant women included in the programme (five of the seven hospitals).

The rate of congenital transmission was calculated as the proportion of children infected of the total number of pregnant women confirmed as positive.

Table 1

Characteristics of hospitals and screening programmes for *Trypanosoma cruzi* infections in pregnant women, Madrid, Spain, January 2008–December 2010

Hospital	Number of beds	Attending population	Number of deliveries (2010)		Start date of screening	Type of screening	Screening tests	Confirmation / Complementary tests[a]
			Total	Endemic zone / Bolivia				
1	1,750	750,000	7,513	1,826 / 443	Jul 2008	Selective[b] (pregnancy or delivery)	ICT[c]	ELISA + IFI / PCR
2	1,328	787,000	6,599	1,359 / 191	Dec 2007	Selective[d] (pregnancy or delivery)	ICT[e]	ELISA + IFI / PCR
3	616	397,083	3,193	272 / 15	Nov 2008	Universal[f] (first trimester)	ICT[c] (Nov 2008-Feb 2010); ELISA[a] +IFI[a] (Feb-Dec 2010)	ELISA + IFI / PCR
4	630	213,654	2,010	81 / 2	Oct 2008	Universal[g] (2008-2009 first trimester; 2010 second trimester)	ELISA[a]+IFI[a]	ELISA + IFI
5	362	264,691	2,288	115 / 3	Jan 2008	Universal[f] (first trimester)	ELISA[a]+IFI[a]	ELISA + IFI / PCR
6	447	189,359	1,647	123 / 6	Feb 2008	Universal[g] (pregnancy or delivery)	ELISA[h]/ ICT[c]	ELISA + IFI / PCR
7	1,136	529,528	2,700	361 / 77[i]	Mar 2008	Universal[g] (pregnancy or delivery)	ICT[g] + ELISA[j]	ELISA + IFI

ELISA: Enzyme-linked immunosorbent assay; ICT: Immunochromatographic test; IFI: Indirect immunofluorescence; PCR: Polymerase chain reaction.

[a] In-house tests at the National Microbiology Centre, Instituto de Salud Carlos III [14].

[b] Pregnant women from Bolivia or risk areas according to maps indicating distribution in particular countries, and pregnant women with any other previous clinical or epidemiological risk.

[c] Simple Stick Chagas (Operon S.A., Zaragoza, Spain).

[d] Only Bolivian pregnant women.

[e] Ab Combo Rapid Test (CTK Biotech. Inc., San Diego, USA).

[f] Pregnant women from Latin America except Cuba and the Dominican Republic.

[g] Latin American women without exceptions.

[h] Bioelisa Chagas (Biokit, Lliça d'Amunt, Spain).

[i] Initially monitored in Hospital 7, delivery in Hospital 1.

[j] Chagas ELISA (Vircell S.L., Granada, Spain).

Results

The characteristics of the hospitals, number of deliveries, start date of screening, type of screening, and both screening and confirmation tests are described in Table 1. Two hospitals carried out the selective serological screening and the rest adopted a universal screening. The proportion of deliveries to women from areas where the disease is endemic over the total number of deliveries attended in 2010 for each hospital, ranged from 4% (81/2,010) in Hospital 4 to 24.3% (1,826/7,513) in Hospital 1 (Table 1). The coverage of monitoring only reached 100% in the hospitals that adopted a universal serological screening programme (all pregnant women from Latin America, without excluding those who came from countries where the disease is not endemic) at any moment during the pregnancy as well as at delivery (Hospital 6 and 7). The hospitals that adopted a universal screening programme systematically applied in the first or second trimester of pregnancy, did not cover pregnant women who were only attended at the time of delivery, Hospitals 3, 4 and 5 (Table 2).

A total of 3,839 pregnant women were tested, and the overall prevalence was 3.96% (152/3,839). The hospitals that adopted a universal screening programme found a prevalence between 0.5% (Hospital 5) and 4.2% (Hospital 7). In contrast, the hospitals that selectively screened only pregnant Bolivian women (Hospital 2) or pregnant Bolivian women plus pregnant women from other countries with clinical and epidemiological background (Hospital 1) registered a prevalence of 10% and 6.2%, respectively (Table 2). The data from Hospitals 1, 2, 3, 4 and 6 which had recorded the country of origin of the pregnant women included in the study identified a prevalence of 11.4% in Bolivian women. Data from hospitals which had not recorded the country of origin indicated a 3.1% prevalence in all the Latin American pregnant women. The prevalence in pregnant women from other countries was not calculated, as the data regarding distribution by country of origin were incomplete (Table 3). The rest of seropositive women were from Argentina, Colombia, Paraguay and Peru. Detectable parasitaemia was present in 44% (27/62) of all the pregnant seropositive women who were tested by PCR (Table 2).

Four infected children were detected and they were all born to Bolivian mothers. Given that 95.4% (145/152) of seropositive mothers were from Bolivia, the overall rate (2.6%) of congenital transmission was similar to that for Bolivians (2.8%). Three of the four children were born asymptomatic and two of them received specific treatment with benznidazole in the hospitals where they were diagnosed. The first child was monitored during 15 months. The parasitological tests were negative after treatment (two months). Serological tests returned a negative result three months after treatment and they remained negative for the whole monitoring period (15 months). The other child was diagnosed in December 2010, parasite clearance was

Table 2

Distribution of the pregnant women included in the study and cases of congenital transmission of *Trypanosoma cruzi* infections by hospital, Madrid, Spain, January 2008–December 2010 (n=3,839)

Hospital	Number of pregnant women						Congenital cases (%)	
	Tested before December 2010	Coverage %	Positive screening test	Confirmed positive[a]	Prevalence[b] %	Positive PCR		
1	257	31[c]/26[d]	30	16 / 18	6.2	7 / 15	2[e]	(12.5)
2	521	100[c]/38[d]	53	52 / 53	10	15 / 40	1[f]	(1.9)
3	292	452	4	4 / 4	1.4	1 / 2	0	(0.0)
4	209	NC	7	2 / 4	1	ND	0	(0.0)
5	219	NC	3	1/ 3	0.5	1 / 1	0	(0.0)
6	639	100[d]	13	6 / 9	0.9	3 / 4	1[g]	(16.7)
7	1,702	100[d]	71	71 / 71	4.2	ND	0	(0.0)
Total	**3,839**		**181**	**152 / 165**	**4**	**27 / 62**	**4**	**(2.6)**

NC: not calculated; ND: not determined.

[a] Number of women confirmed as positive compared to those pregnant women with a positive result in the screening.

[b] Calculated from the number of pregnant women confirmed as positive out of the total number of pregnant women tested.

[c] Based on the number of pregnant women tested out of the total number of deliveries to Bolivian women (selective screening).

[d] With respect to the total number of pregnant women from areas where infection is endemic (universal screening).

[e] Diagnosed using PCR and direct observation.

[f] Diagnosed using microhaematocrite and PCR.

[g] Diagnosed using PCR in two independent samples.

obtained one month after treatment and in March 2011 serology was still positive. This child is currently under serological monitoring. The mother of the third asymptomatic child moved to another region where the treatment and follow-up were completed. The fourth child was born with Down's syndrome and congenital cardiopathy. It was treated first with benznidazole, and then with nifurtimox. After recovering from *T. cruzi* infection, it died suddenly at the age of nine months.

Discussion

According to estimates from the Pan American Health Organization (PAHO), the number of people infected with *T. cruzi* in Latin America has come down from the 20 million that they estimated in the 1980s to 8 million in 2005 [16]. This reduction is believed to have been achieved due to the different control initiatives that have been set up (Southern Cone Initiative to Control/ Eliminate Chagas Disease - INCOSUR, Initiative of the Andean Countries to Control Vectoral and Transfusional Transmission of Chagas Disease - IPA, Andean´s Countries Initiative for controlling Chagas disease - ICA and Initiative of the Amazon Countries for Surveillance and Control of Chagas Disease - AMCHA) and the commitment of the governing authorities in each of the countries involved.

Table 3

Distribution and prevalence of *Trypanosoma cruzi* infection in pregnant women by country of origin, Madrid, Spain, January 2008–December 2010 (n=3,839)

Country of origin	Number (%)	Number of confirmed positive cases	Prevalence %
Colombia	239 (13.3)	0	0
Ecuador	379 (21.1)	0	0
Peru	192 (10.7)	0	0
Venezuela	18 (1)	0	0
Brazil	39 (2.2)	0	0
Bolivia	798 (44.4)	91	11.4
Chile	15 (0.8)	0	0
Paraguay	60 (3.3)	0	0
Argentina	17 (0.9)	0	0
Nicaragua	4 (0.2)	0	0
Other	38 (2.1)	0	0
Total pregnant women from countries where the disease is endemic	1,799 (100)	91	5.1
Total pregnant women from countries where the disease is not endemic	59 (100)	0	0
Data not available[a]	1,981 (100)	61[b]	3.1
Total	**3,839 (100)**	**152**	**4**

[a] Hospitals that did not collect information on the country of origin.

[b] Includes pregnant women from: Bolivia (n=54); Argentina (n= 1); Paraguay (n=1); Colombia (n=2); Peru (n=2) and of unknown origin (n=1).

In the past, Spain has registered cases associated with the three main modes of infection in non-endemic regions: transfusion of blood products [7,8], organ transplantation [17] and vertical transmission [18-20] At present, according to the Royal Decree 1088/2005 [4], blood donations from donors who come from areas considered to be at high risk, or with a history of being exposed to high risk, must be tested in order to avoid the use of contaminated blood. The same measures were adopted by the Spanish National Transplant Organization [21,22]. However, there are no national regulations in Spain for the monitoring of pregnant women from areas where the disease is endemic.

This paper shows that, given the absence of regulations, each hospital adopted a screening programme that fitted its own organisation and facilities, and this means that the current monitoring programmes have variable coverage.

Despite the lack of homogeneity, according to the data collected, the observed overall prevalence of seropositive pregnant women coming from endemic areas for Chagas disease of 3.9% (152/3,839) was similar to that described in hospitals in Catalonia and Valencia: 3.4% (46/1,350) and 4.7% (29/624), respectively. However, the prevalence reported here among pregnant Bolivian women in Madrid (11.4%) was lower than that reported in other studies carried out in Catalonia and Valencia, 22% (42/46) and 17.5% (24/29), respectively [18,23]. As in those studies, the pregnant women who tested positive generally came from Cochabamba and Santa Cruz, regions in Bolivia where the disease is hyperendemic. Since data were not collected on pregnant Bolivian women who tested negative, it is probable that the difference in prevalence between regions in Spain reflects the origin of the Bolivians living in those regions and the prevalence in those areas of origin [24]. On the other hand, the overall rate (2.6%) of congenital transmission found in Madrid was lower than that reported in Catalonia (7.3%) [18], although the proportion of pregnant women with detectable parasitaemia was similar (27/62 in Madrid compared with 18/35 in Catalonia). Taking our data into account, it can be concluded that there are two possible screening options: (i) screen only pregnant Bolivian women (the high-risk population), or (ii) screen all pregnant women from areas where the disease is endemic. In 2008 when the programme began, there were insufficient automatic high-throughput serological tools, but this situation has changed in the recent years. At present, testing pregnant women for *T. cruzi* antibodies when they first come into contact with the healthcare system, would represent a cost of approximately EUR 2 each, if this test is added to the tests for ToRCHeS syndrome (Toxoplasma, Rubella, Cytomegalovirus, Herpes simplex, syphilis, HIV). Taking into account the data in Table 3, the screening of the 798 Bolivian women would have costed EUR 1,596 for the three years. This means that the detection of one congenital case would cost on average EUR 399. If universal screening was carried

out, the detection of one congenital case would cost EUR 1,920 (3,839 x EUR 2 / 4 congenital cases). Thus, selective screening of pregnant Bolivian women is more cost-effective than screening all pregnant women from areas where the disease is endemic. However, it is important to highlight that cases of congenital infection were also reported in children born to Argentinean mothers [19,20]. If screening is not carried out under either of these protocols, the question would remain on the cost to be incurred by the healthcare system for the treatment of 30% to 50% of these children who would develop severe forms of Chagas disease in the future.

Furthermore, the monitoring of pregnant women also offers the possibility of detecting other adult family members for the first time, together with the detection of children whose condition was previously overlooked. According to data from one of the hospitals included in this study, between three and five affected family members can be detected together with every pregnant infected woman identified (E Vilalta, personal communication, February 2011). As the immigrant population is predominantly composed of young adults [18,23] monitoring pregnant women would facilitate not only the treatment of infected children, but also the passive detection of the relatives and the other infected immigrants who could be treated. Thus, universal serological screening is an important ethical requirement and would still prove to be cost-effective by reducing the risk of developing severe illness that may result from infection.

Conclusion

Monitoring of pregnant women only reaches full coverage if universal screening of pregnant women from Latin America is carried out at any moment of pregnancy, including the delivery. A common national regulation is necessary in order to ensure homogenous implementation of screening. Thus, newborns can be cured if they are treated at an early stage of the disease.

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Working Group on Chagas Disease of Autonomous Community of Madrid

Alfredo Pérez, Servicio de Microbiología, Hospital de Móstoles
Beatriz Orden, Servicio de Microbiología, Hospital Universitario Puerta de Hierro
Carmen Betriu, Servicio de Microbiología, Hospital Clínico de San Carlos
Carmen Cañavate, Servicio de Parasitología, Centro Nacional de Microbiología, ISCIII
Daniel Blázquez, Servicio de Pediatría, Hospital Clínico San Carlos
Efrén Salto, Servicio de Microbiología, Hospital 12 de Octubre
Encarna Villalta, Consulta del Viajero, Hospital Gregorio Marañón
Francisco J Merino, Servicio de Microbiología y Parasitología, Hospital Universitario Severo Ochoa de Leganés
Gerardo Rojo, Servicio de Medicina Interna, Hospital Príncipe de Asturias
Iciar Olabarrieta, Neonatología, Hospital Universitario Severo Ochoa de Leganés
Isabel Camaño, Obstetricia y Ginecología, Hospital 12 de Octubre
José Beceiro, Servicio de Pediatría/Neonatología, Hospital Príncipe de Asturias
Juan Cuadros, Servicio de Microbiología y Parasitología, Hospital Príncipe de Asturias
Laura Molina, Laboratorio Microbiología, Centro Hospital Fundación Alcorcón
Luis Ignacio González-Granado, Servicio de Pediatria, Hospital 12 de Octubre
Manuel del Álamo, Servicio de Microbiología y Parasitología, Hospital Universitario Severo Ochoa de Leganés
María Cruz Estévez, Servicio de Ginecología y Obstetricia. Hospital Príncipe de Asturias
María del Mar Santos, Sección Enfermedades Infecciosas, Servicio de Pediatría, Hospital Gregorio Marañón
María Flores, Servicio de Parasitología, Centro Nacional de Microbiología, ISCIII
María Penin, Servicio de Pediatría, Hospital Príncipe de Asturias
María Rocío Martínez, Servicio de Microbiología, Hospital Universitario Puerta de Hierro
Maribel González, Servicio de Pediatría, Hospital 12 de octubre
Marta Llorente, Servicio de Pediatría, Hospital Príncipe de Asturias
Nuria Girones, Departamento de Parasitología, Centro de Biología Molecular Severo Ochoa
Pablo Rojo, Departamento de Pediatría, Hospital 12 de Octubre
Paloma Merino, Servicio de Microbiología, Consulta de Medicina Tropical, Hospital Clínico de San Carlos
Pedro Jiménez, Sección de Obstetricia, Hospital de Príncipe Asturias
Rosario Millán, Servicio de Microbiología y Parasitología, Hospital Universitario Puerta de Hierro
Silvia García, Servicio de Microbiología y Parasitología, Hospital La Paz
Teresa Gastañaga, Ginecología, Hospital Clínico de San Carlos
Teresa Garate, Servicio de Parasitología, Centro Nacional de Microbiología, ISCIII

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