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*Emerging Problems in Infectious Diseases*

# Chagas disease prevalence in pregnant women: migration and risk of congenital transmission

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## Abstract

Introduction: Argentina has been a preferential target for Bolivian immigrants for decades. The relatively recent migratory flux includes Germany, France, the United States, Australia, Japan, and some Latin American countries. The aim of this cross-sectional study was to describe the prevalence of Chagas disease in pregnant women, analyzing the Bolivian-specific Chagas prevalence as the main contributor of migratory populations from Chagas disease-endemic areas to Buenos Aires city, Argentina, and to evaluate the impact of these migrant influxes on the process of the "urbanization" of the disease in reference hospital José Maria Ramos Mejia (JMRM).

Methodology: Overall, 21,332 pregnant women (100%) between 15 and 49 years of age derived from the public maternity service of JMRMH were studied. Serology data was obtained from registered serological diagnosis data, consisting of three different serological tests performed at the Public Parasitology Unit.

Results: Although general prevalence decreased during the analyzed period, the specific prevalence of pregnant women from Bolivian origin showed a sustained growth during 1983–2013. Solely 5% of the total pregnant women population from Bolivia contributed to one third of the total Chagas prevalence.

Conclusions: This study showed that a cohort of pregnant women from Bolivia who attended JMRMH during the period 1983–2007 constituted a population at risk for congenital transmission. Increased migration from endemic areas of Bolivia might potentially increase the prevalence of Chagas disease among pregnant women. In addition, this study highlights the importance to analyze specific prevalence according to endemic areas to determine the profiles of potential hidden prevalence.

**Key words:** prevalence; migration; congenital transmission; pregnant women.

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## Introduction

The Brazilian physician Carlos Chagas, who named the parasite *Trypanosoma cruzi*, discovered Chagas disease in 1909. Owing to the parasite's distribution throughout Central and South America, this disease is commonly known as American trypanosomiasis. It causes more deaths in the Americas than does any other parasitic disease.

Estimates derived from the World Health Organization (WHO) indicate that in Latin America, 16 to 18 million people are already infected with *Trypanosoma cruzi* and some 90 million are at risk of infection. This represents an average prevalence of 4%; however, in some regions, the local prevalence can exceed 75% [1].

In the past, vector transmission of *T. cruzi* has generated the greatest number of cases of Chagas disease in Argentina. The vector control programs implemented in the last decades in Argentina showed that 4 of 18 provinces were officially declared to be Chagas free [2].

Moreover, as is generally agreed, even when full control of vector transmission has been achieved, congenital infections remain a major health problem. The prevalence of *T. cruzi* infection in pregnant women is within the expected values for endemic countries of Latin America (between 2% and 51%). It is currently estimated that between 2% and 8% of infected pregnant women transmit the parasite to their newborns in Latin America [3,4]. In fact, some authors estimate that there will be new cases of congenital Chagas for over 30 years [2]. In Argentina, the prevalence of pregnant women infected with the parasite decreased by 8% from 1995 to 2009 (Figure 1). Nevertheless, every year, there

are around 1,300 new cases of infants born with the disease in Argentina [5].

Considering all the possible clinical presentations, congenital Chagas disease is the one that demands the most rapid and sensitive diagnostic methods [5,6]. Conventional serology has no diagnostic benefit for the first six months of life. In addition, it should be noted that at this stage, treatment could lead to complete cure. Diagnosis during pregnancy and risk characterization of a given population should be seen as a window of opportunity for inquest cases of congenital Chagas [4,7,8]. The healing of congenital Chagas disease in this critical age depends on detection during pregnancy, early diagnosis in the neonate, and quick treatment [5,9].

The city of Buenos Aires received a large influx of immigrants from the north of the country and neighboring countries with a high prevalence Chagas, such as Bolivia and Paraguay [6]. In terms of comparative employment opportunities, some countries constitute attractive targets for millions of poverty-stricken immigrants. In view of this, we decided to survey pregnant women by origin to assess the evolution of the prevalence to find out which populations are at risk of congenital transmission. Although there are some isolated studies related to migration and prevalence [7, 9-14], they have not assessed the impact of a specific population over the total prevalence among pregnancies during sufficiently long periods to allow for an evolutionary analysis.

This cross-sectional study was oriented to determine the evolution of prevalence of Chagas disease in pregnant women attending José Maria Ramos Mejia hospital (JMRMH) during the period between 1 January 1983 31 December 2007. In addition, the risk profile of the pregnant population was studied.

## Methodology

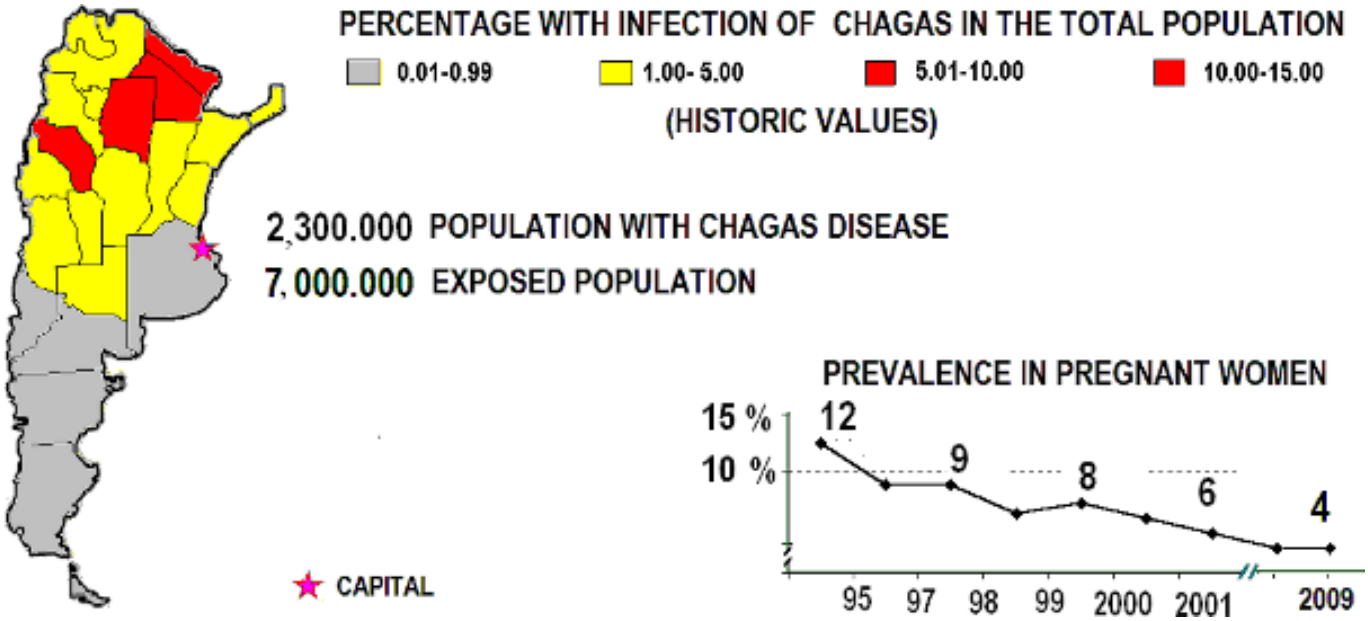
*Study population*

Buenos Aires is the capital and largest city of Argentina, and the second-largest metropolitan area in South America. It is located on the western shore of the estuary of the Río de la Plata, on the continent's southeastern coast. The Greater Buenos Aires conurbation, which also includes several Buenos Aires province districts, constitutes the third-largest conurbation in Latin America, with a population of around 15.5 million. All pregnant women between 15 and 49 years of age derived from the public maternity service who attended JMRMH for the first time during the period between 1 January 1983 to 31 December 2007 were subjected to pregnant controls for Chagas (100%). It is important to note that most Bolivians patients controlled in JMRMH are known to live mainly in the greater northeast area of the Buenos Aires state border and in proper localities from Buenos Aires city (CABA) near the reference hospital.

*Procedure and questionnaire*

A questionnaire was used to collect information about demographic characteristics and potential factors

**Figure 1.** Diagrammatic representation of situational state of Chagas Disease in Argentina. Source: Adapted from National Coordination for Vectors Control report for 1994–2001 and http://www.msal.gov.ar/chagas/index.php/ for the prevalence for 2009.



associated with Chagas infection. The demographic characteristics included age and residence region. The potential factors associated with Chagas infection included history of transfusion and having Chagas-positive family members. Additional data obtained from pregnant women included more detailed data about their country, including state or province of origin, and type of housing.

*Serology testing*

All pregnant women with discordant serology were excluded. Blood samples were obtained for determination of serological diagnosis using serological tests such as indirect hemagglutination (HAI), enzyme-linked immunosorbent assay (ELISA) (M Wiener Laboratories S.A.I.C. Rosario, Argentina), and indirect immunofluorescence (IFA) (IFI -Inmunofluor Chagas Biocientífica SA, Buenos Aires, Argentina). Using two serological reactions allowed a sensitivity range between 98% and 99.5% to be achieved. These are the classic laboratory diagnosis methods based on procedures according to the WHO criteria. The serological method offers an accurate diagnosis in the chronic indeterminate phase of the disease.

Newborns whose mothers had positive tests during pregnancy were assessed by direct parasitological micromethod to detect trypomastigotes by means of direct microscopy of a microhematocrit adapted from Woo *et al.* [15].

*Statistical analysis*

The results were analyzed by applying the statistical procedure called join point, a software regression study provided by the Surveillance Research Program of the USA National Cancer Institute (http://srab.cancer.gov/joinpoint) that enables the assessment of the significance of the prevalence changes observed (rate of change) in the percentage of prevalency in each group during the above-mentioned period. The aim of this analysis was to identify potential points where a significant change in the linear slope of the trend (in a log scale) occurred. In join point analysis, the best-fitting points, called join points, were chosen according significant rate changes. The analysis starts with the minimum number of join points (*e.g.*, zero join points), and tests whether one or more join points are significant. Each significant join point indicates a change in the slope (if any). To describe linear trends by period, the estimated annual percent change is then computed for each of those trends by fitting a regression line into the natural logarithm of the rates using calendar year as a regressor variable. The use of the join point software for analysis has allowed a detailed and accurate description of the pattern of prevalence along the period, since it identifies the calendar years in which statistically significant changes in trends occurred. This offers a clearer picture of actual trends in prevalence over long periods.

*Ethical considerations*

This study met the ethical standards and was approved by the ethics committee of JMRMH.

## Results

Overall 21,332 pregnant between 15 and 49 years of age were studied. A total of 869 were seropositive and 20,463 were seronegative. In all cases HAI, IFA, and ELISA confirmed seropositivity. From 869 seropositive patients derived from diverse Latin America countries and Argentina localities, 274 pregnant women were of Bolivian origin.

The total average prevalence of Chagas disease among pregnant women in the period was 4.1%. A high percentage of Bolivian women (274/325; 84.3%) controlled in JMRMH were Chagas positive (Table 1).

Although a relatively low percentage of pregnant women from Bolivia (1.5%) were controlled in JMRMH during 1983–2007, they represented 31.5% of the total prevalence (Table 2).

Statistically significant join point results were obtained only with zero join points in both groups (Bolivian origin and total prevalence groups). Trends for one period between Bolivian origin and total pregnant women were compared. The analysis of the prevalence of Chagas disease in the total population of pregnant women indicated a significant decline from 2.2% (annual percent change) for the entire period ($p < 0.05$, obtained with zero join points) (Figure 2), in line with national tendencies.

**Table 1.** Percentage of Chagas-positive and -negative pregnant patients according to their origin.

| Origin | Ch + | Ch- |
|---|---|---|
| Bolivian patients | 84.3 | 15.7 |
| Non-Bolivian patients | 2.8 | 97.2 |
| **Total** | **4.1** | **95.9** |

Source: Parasitology Unit from JMRMH. Period 1983 to 2007.

**Table 2.** Relative percentage of seropositive and seronegative pregnant patients from Bolivian and non-Bolivian origin.

| | Ch + | Ch- | Total % |
|---|---|---|---|
| Bolivian origin | 31.5 | 0.2 | 1.5 |
| Non-Bolivian origin | 68.5 | 99.8 | 98.5 |
| **Total** | **100.0** | **100.0** | **100.0** |

Source: Parasitology Unit from JMRMH. Period 1983 to 2007.

**Figure 2.** Evolution of the prevalence in the Bolivian origin (BO) group. Join point of prevalence of Chagas disease in the BO pregnant population was statistically significant for one period ($p < 0.05$). Source: Parasitology Unit from JMRMH. Period 1983 to 2007.

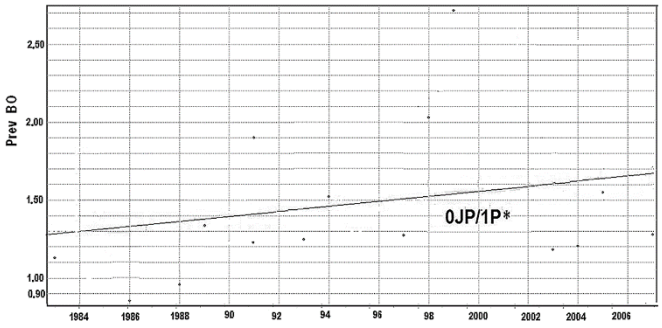
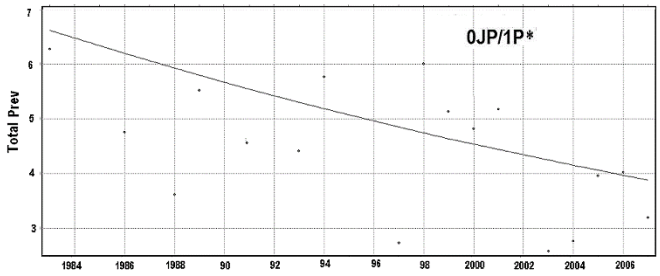



**Figure 3.** Evolution of the prevalence in the total pregnant women. Join point of prevalence of Chagas disease in the total pregnant population was statistically significant for one period ($p < 0.05$). Source: Parasitology Unit from JMRMH. Period 1983 to 2007.




In contrast, prevalence of Chagas disease in women of Bolivian origin shows a progressive increase along the period. The best-fitted model adjust was obtained with zero join points (Figure 3), which was statistically significant for one period ($p < 0.05$).

Taken together, these results indicate that Chagas disease prevalence in Bolivian pregnant women contributed to one third of congenital transmission risk during the period 1983–2007

The frequencies of the department, province, or locality of origin of Chagas-positive pregnant Bolivian women showed that they came from endemic areas of medium and high risk for Chagas infection areas (Figure 4, Table 3).

**Figure 4.** Risk stratification at the community level in endemic areas. Bolivia, 2008. Source: Adapted from Chagas Program, Ministry of Health and Sports (MHS). Bolivia. (www.sns.gob.bo)

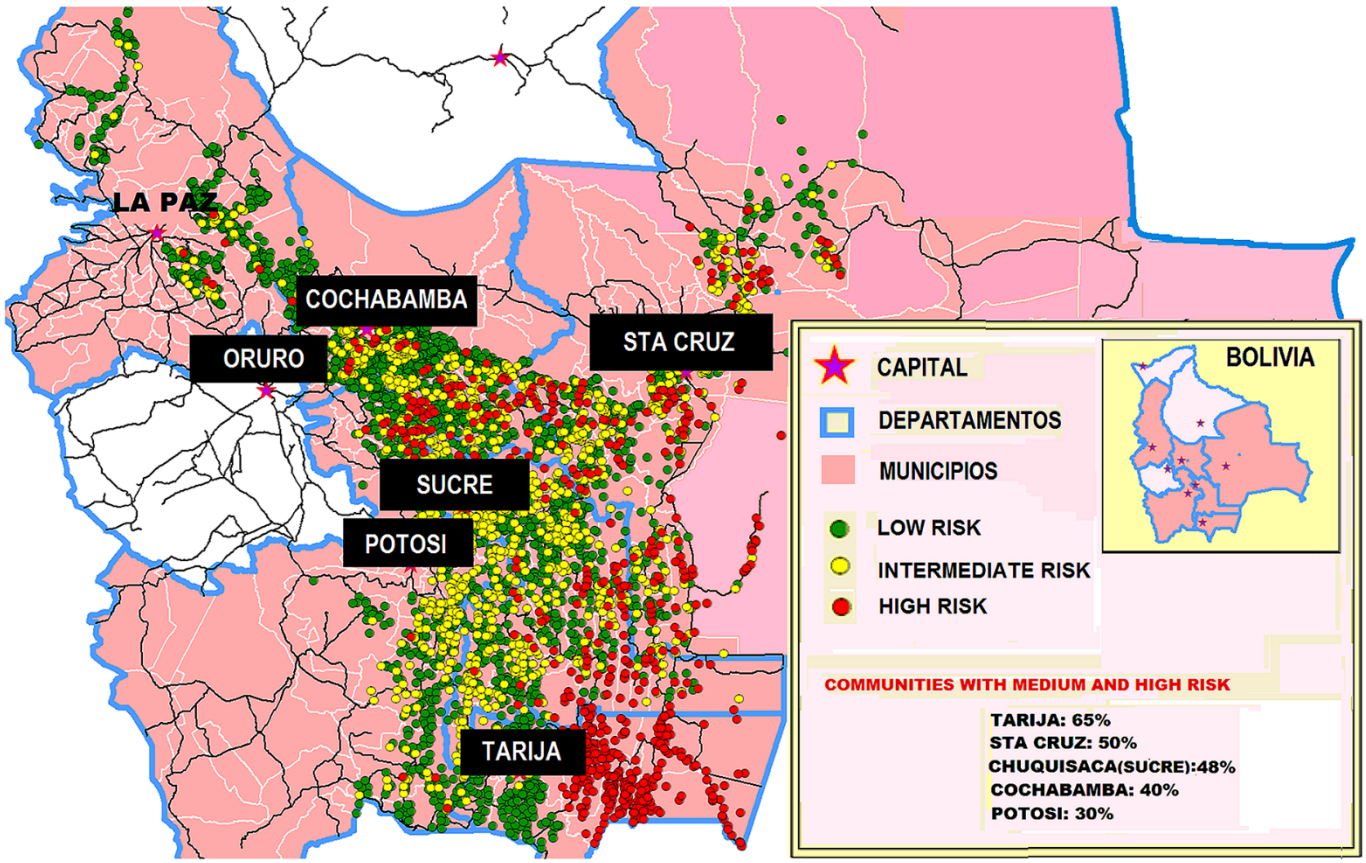


**Table 3.** Annual total cases and percentage of Chagas-positive pregnant patients from Bolivia in José Maria Ramos Mejia Hospital according to their localities of origin.

| | 1983 | 1986 | 1988 | 1989 | 1990 | 1991 | 1993 | 1994 | 1997 | 1998 | 1999 | 2000 | 2001 | 2003 | 2004 | 2005 | 2006 | 2007 | Freq. | % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Cochabamba | 7 | 4 | 3 | 7 | 9 | 12 | 6 | 8 | 4 | 6 | 4 | 15 | 11 | 4 | 8 | 12 | 10 | 5 | **135** | **41.5** |
| Sta Cruz | 1 | 3 | 3 | 4 | 2 | 3 | 2 | 3 | | 3 | 2 | 3 | 5 | | 3 | 5 | 7 | 3 | **52** | **16** |
| Sucre | | | | | | | | | | | | 5 | 5 | 1 | 1 | 1 | 1 | 5 | **19** | **5.85** |
| Tarija | | | | | | | | | | | 1 | 2 | 2 | | | | 3 | 3 | **11** | **3.46** |
| Yacuiba | | | 2 | | | | | 1 | | | | | 1 | | | | 2 | | **6** | **1.85** |
| Potosi | | | | | | 1 | | | | 1 | 5 | | 2 | 1 | 2 | | 2 | 3 | **17** | **5.2** |
| Oruro | | | | | | | | | 2 | | | | | | | | | | **2** | **0.61** |
| Unspecified | 1 | | 1 | 2 | 2 | 1 | 5 | 1 | 8 | 11 | 15 | 4 | | 10 | 3 | 10 | 2 | 7 | **83** | **25.53** |
| **TOTAL** | **9** | **7** | **9** | **13** | **13** | **17** | **13** | **13** | **14** | **21** | **27** | **29** | **26** | **16** | **17** | **28** | **27** | **26** | **325** | **100** |

Source: Parasitology Unit from JMRMH. Period 1983 to 2007.

## Discussion

Bolivia has unique characteristics in terms of the prevalence of Chagas e disease [4], with a high prevalence in almost all locations (Table 4). The analysis of the trend in the prevalence of Chagas disease diagnosed in pregnant women during the period 1983–2007 clearly showed that while the overall prevalence of the disease was significantly reduced, the prevalence of disease in pregnant women of Bolivian origin increased significantly over the period.

The analysis of the different places of origin from Bolivian pregnant women (provinces, departments, or other minor locations) who attended HJRMH showed a variety of endemic localities (Table 3). The Department of Cochabamba yielded the largest average number of Chagas-positive cases during the study period (Table 3). Importantly, many Bolivian immigrants did not provide information about their site of origin. This group is indicated as "unspecified" in Table 3. Since this group is numerically relevant, it is difficult to conclude that the localities of origin reported by patients were representative in terms of its percentage contribution of the locations of reference, except probably in the case of Cochabamba as the main contributor. Despite this restriction, results suggest that the locations of origin reported by patients are mostly endemic areas of medium and high risk. An exception to this is provided by the Department of Oruro, which is not an endemic area (Figure 4, Table 3).

This study is restricted due to the limitations intrinsic to cross-sectional studies in establishing causal relationships. Higher prevalence in Bolivian pregnant women seems to be the result of two main factors: higher intrinsic prevalence in localities of origin and preferential migratory urban targets, including the northwest area of Greater Buenos Aires near the CABA border and HJMRM-associated geographic areas. This study cannot be taken to show the current epidemiology of Chagas disease in urban hospitals in Argentina or all the hospitals in Buenos Aires city. Our survey was restricted to the influence area of JMRMH, and the total prevalence seems to be representative of the study site

**Table 4.** Prevalence of Chagas disease in pregnant women in Bolivia according representative studies during the period of infectious diseases.

| Author | Year | County | Type of population | Seroprevalence |
|---|---|---|---|---|
| Zuna *et al.* | 1979 | Abapo | Itinerant | 81% |
| SNS-CCH | 1991 | Chuquisaca | Farm | 78.1% |
| Romero *et al.* | 1977 | Gutiérrez | Itinerant | 70% |
| SNS-CCH | 1991 | Tarija | Farm | 60.5% |
| Azogue E | 1993 | Santa Cruz | City | 54% |
| Zuna *et al.* | 1978 | Santa Cruz | Suburban | 54% |
| Azogue *et al.* | 1985 | Santa Cruz | City | 51% |
| SNS-CCH | 1991 | Cochabamba | Farm | 46% |
| Jijena *et al.* | 2001 | Tarija | City | 43.1% |
| Brutus *et al.* | 2002–2004 | Yacuiba | Rural | 42,6% |
| Leyton W | 1999–2000 | Tarija | City | 40.2% |
| Jijena *et al.* | 2000 | Tarija | City | 40.5% |
| Jijena *et al.* | 2002 | Tarija | City | 38.4% |
| Roca, *et al.* | 1996 | Santa Cruz | City | 30,6% |
| Torrico *et al.* | 1992–1994 | Cochabamba | City | 27.6% |
| Torrico *et al.* | 1997–2001 | Cochabamba | City | 17.3% |

SNS-CCH: Bolivian National Health System of Control of Chagas.

area of the attending pregnant women, but is not representative of the entire territory of Buenos Aires city or Argentina, although national values of total prevalence were similar (4% versus 4.1%). Our study indicated that 31.5% of seropositive pregnant women, all of whom were confirmed to have the infection, had come from Bolivia.

This means that a relatively low percentage (1.5%) of Bolivian pregnant women from the total population controlled in JMRMH during the 1983–2007 period contributed to one third of the total prevalence. In addition, with respect to the specific prevalence contribution of Chagas disease from women of Bolivian origin who were pregnant during the period 1983–2007, the trend line indicates a sustained and significant increase over the period. Newborns of Chagas-positive mothers are more likely to get infected and become chronic carriers due their higher prevalence. The prevalence in pregnant women according to 16 selected studies (Table 4) is extremely high in Bolivian localities, averaging 44,5% of the total women population, 50% of them indicate a prevalence range from 38.8% to 58.9%.

Our results seem to be caused by the combination of two main factors: high Chagas prevalence in pregnant women in Bolivia (Table 4) and a sustained rate of growth of Bolivian immigration over the last 30 years to specific areas in Argentina. JMRMH is probably the hospital in Buenos Aires city that receives more Bolivian immigrants, based on demographic data of radication (data not shown).

Migrants need to be offered the same access to healthcare services as the rest of the population. It is also important to do more to eradicate infectious disease in developing countries in order to reduce the global burden of disease

## Conclusions

Our results indicate that a very low percentage (1.5%) of Bolivian pregnant women from the total population that attended JMRMH during 1983–2007 contributed to one third of the total prevalence. This study clearly demonstrates that Bolivian pregnant women are a population at high risk of congenital transmission, noting the importance of public policies in order to recruit pregnant Bolivian women to the JMRMH to improve their health profiles, underlining the need for treatment of congenital Chagas close after pregnancy serological controls.

This procedure makes it feasible to achieve parasitological and serological cure with parasiticidal drugs in almost all cases of congenital Chagas disease. It is also important to note that these results reinforce the hypothesis that increased migration from endemic areas of Bolivia could increase the specific prevalence of Chagas disease in pregnant women in some hospitals located in Greater Buenos Aires and CABA that, in view of the general prevalence reduction along the period, could well be underestimated. Epidemiological surveillance strategy must be based on focusing on the serological control of specific risk groups according its immigration origin from endemic biogeography's areas, to avoid the occurrence of new cases of congenital Chagas disease.

### Authors' contributions

Rodolfo A. Kölliker-Frers and Iván Insua contributed equally to this work.

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