



Vertical transmission of HIV-1 in the western region of the State of São Paulo

Transmissão vertical do HIV-1 na região oeste do Estado de São Paulo

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ABSTRACT

Introduction: This study aimed to determine the prevalence of vertical HIV-1 transmission in the western region of the State of São Paulo, Brazil. **Methods:** The study analyzed the medical records of HIV-1-infected mothers and infant pairs living in the municipalities of São Paulo Regional Health Departments DRS II (Araçatuba) and DRS XI (Presidente Prudente). From March 2001 to March 2006, blood samples were collected and referred to the Molecular Biology Unit of the Adolfo Lutz Institute (ALI), Presidente Prudente. HIV-1-RNA viral load was determined by bDNA assay. **Results:** The number of births (109/217, 50.2%) and vertical HIV-1 transmissions (6/109, 5.5%) that occurred in DRS II was similar to births (108/217, 49.8%) and vertical transmissions (7/108, 6.5%) in DRS XI ($p > 0.05$). Although 80% (4/5) of the infected children were male in DRS II, while in DRS XI, 75% (6/8) were female, no differences between sex regarding infected and noninfected children in the regions of Araçatuba and Presidente Prudente were verified. The overall vertical HIV-1 transmission rate was 6%. No consistent reduction in the prevalence of vertical HIV-1 transmission occurred over the years. About 20% of mothers did not know the HIV-1 status of their newborns eight months after delivery. **Conclusions:** In the present study, MTCT prevalence rates were about 70% higher than those previously determined in the State of São Paulo, with no reduction throughout the period. Furthermore, a significant number of mothers did not know the HIV-status of their newborns eight months after delivery.

Keywords: HIV-1. Vertical transmission. Brazil.

RESUMO

Introdução: O objetivo desse estudo foi determinar a prevalência da transmissão vertical do HIV-1 na região oeste do Estado de São Paulo, Brasil. **Métodos:** Foram analisadas as fichas de mães infectadas pelo HIV-1 e recém-nascidos, residindo em municípios das Delegacias Regionais de Saúde (DRS II, Araçatuba) e (DRS XI, Presidente Prudente). Entre março de 2001 e março de 2006 as amostras foram colhidas e enviadas ao Instituto Adolfo Lutz, Presidente Prudente. A carga viral do RNA-HIV-1 foi determinada por bDNA. **Resultados:** O número de nascimentos, 50,2% (109/217) e a transmissão vertical do HIV-1, 5,5% (6/109) ocorrido na DRS II foi semelhante aos nascimentos, 49,8% (108/217) e a transmissão vertical, 6,5% (7/108) ocorrido na DRS XI, respectivamente. Embora na DRS II, 80% (4/5) das crianças infectadas fossem meninos e na DRS XI, 75% (6/8) meninas, não houve diferença entre sexo em crianças infectadas ou não nas regiões de Presidente Prudente e Araçatuba. A taxa de transmissão vertical para o HIV-1 foi de 6%. Não houve diminuição da taxa de infecção ao longo dos anos. Cerca de 20% das mães não haviam feito exame para HIV-1 de seus filhos oito meses após o nascimento. **Conclusões:** A transmissão vertical para HIV-1 foi cerca de 70% maior que a encontrada anteriormente no Estado de São Paulo, sem diminuição ao longo do período. Além disso, um número expressivo de mães não realizou exame de seus filhos oito meses após o nascimento.

Palavras-chaves: HIV-1. Transmissão vertical. Brasil.

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INTRODUCTION

An estimated 33.4 million people live with HIV-1 worldwide, 2 million of whom live in Latin America. Although epidemiological data suggest that the HIV-1 epidemic remains stable in the region, over the last decade, there has been an increase in the incidence of HIV/AIDS among women. Since most of the infected women are of reproductive age, another branch of the expanding HIV-1 epidemic is vertical transmission of the virus¹. The majority of neonates acquire the infection through mother-to-child transmission (MTCT) inside the uterus, during labor or delivery, or by breastfeeding².

Brazil was one of the first developing countries to implement measures to prevent MTCT of HIV-1. The results of these efforts have manifested in an important reduction in vertical transmission rates, from 20%-30%, detected in studies prior to antiretroviral prophylaxis, to 2%-5% in more recent years^{3,4}. In developing countries, hospitals and public health centers are not appropriately equipped to diagnose and treat women at risk of HIV-1-infection, resulting in higher levels of vertical transmission.

The State of São Paulo is divided into Regional Health Departments, with each region harboring several small municipalities. Strategically located in the city of the Regional Health Department, Public Reference Laboratories are responsible for confirming HIV tests and for determining viral load counts in HIV-1-positive pregnant women and infant pairs. Epidemiological data are of interest and should contribute to the development of local and national policies to prevent and control MCTC. However, there are few specific studies addressing this issue in the western region of State of São Paulo. The study aimed to determine vertical HIV-1 transmission rates in the western region of State of São Paulo.

METHODS

State of São Paulo is divided into 17 Regional Health Departments governed by local and regional public health authorities. Located in the western part

of Southeast Brazil, the Regional Health Department of Araçatuba (DRS II) is composed of 40 municipalities with approximately 760,000 inhabitants. The Regional Health Department of Presidente Prudente (DRS XI) is composed of 45 municipalities, with approximately 700,000 inhabitants, who mainly live in small cities and rural communities. This is a descriptive and retrospective study that analyzed the medical records of mothers and infant pairs referred to the Molecular Biology Unit of the Medical Biology Section of the Adolfo Lutz Institute (ALI), the public reference laboratory of the State of São Paulo, by DRS II and DRS XI. All mothers participating in the study presented HIV-1-positive serology by enzyme-linked immunosorbent assay (ELISA) and the results were confirmed by either western blot or indirect immunofluorescence assay.

Blood samples were collected from 217 infants born of HIV-1-infected mothers, from March 2001 to March 2006, living in the municipalities under the DRS II and DRS XI. The samples were submitted to HIV-1-RNA viral load determination by the ALI. The inclusion criteria were as follows: I) exposed children whose blood samples were forwarded to the ALI for HIV-1-RNA determination, with the aim of assisting in the diagnosis of MTCT; II) children up to 18 months of age at the first HIV-1-RNA viral load determination.

bdNA assay

Quantification of HIV-1-RNA was performed on plasma from newborns of HIV-1-positive mothers using the Chiron Quantiplex version 3bdNA assay (Bayer Corporation, Emeryville, California, USA), in accordance with the manufacturer's instructions. The quantitative detection limits ranged from 50 to 500,000 copies/ml. The assays were determined twice after a follow-up period of at least 8 month between the initial and follow-up analysis. This protocol is in accordance with the Brazilian STD/AIDS program^{5,6}. Newborns were considered noninfected when at least two independent blood samples were below the limit of detection of the HIV-1-RNA quantification test. Children were considered infected when at least two independent blood samples were positive for HIV-1-RNA quantification tests. Children older than 18 months were excluded ($n = 3$)⁵.

Statistical analysis

Fisher's exact test and the Chi square test were used to analyze data via GraphPad Instat software (V4.0, San Diego, CA). All p values are two-tailed; p values < 0.05 were considered to be statistically significant. Vertical HIV-1 transmission was calculated as the ratio of the number of newborns with a known HIV-1-positive diagnosis, divided by the total number of newborns.

Ethical considerations

The protocol for this study was approved by the Ethics Committee of the Adolfo Lutz Institute, SP, Brazil.

RESULTS

The number of births (109/217, 50.2%) registered and vertical HIV-1 transmissions (6/109, 5.5%) determined in DRS II was similar to registered births (108/217, 49.8%) and vertical HIV-1 transmissions (7/108, 6.5%) determined in DRS XI ($p > 0.05$). Although in DRS II, 80% (4/5) of the infected children were male, while in DRS XI, 75% (6/8) were female, no differences between sex in infected and noninfected children in the regions of Araçatuba and Presidente Prudente were verified ($p > 0.05$). The overall vertical HIV-1 transmission rate in DRS II and DRS XI was 6% (13/217) (Table 1).

TABLE 1 - Vertical HIV-1 transmission at the DRS II of Araçatuba and the DRS XI of Presidente Prudente, State of São Paulo.

Variable	DRS II	DRS XI	All
Birth (n)	109	108	217
Infection status			
noninfected	103	101	
infected	6	7	
Transmission rate (%)	5.5	6,5	6.0
Sex			
male			
noninfected	55	50	105
infected	4	1	5
female			
noninfected	48	50	98
infected	2	6	8

DRS: Regional Health Departments.

A consistent reduction in the prevalence of vertical HIV-1-transmission rates was not observed throughout the period in the DRS II and DRS XI regions, with the rate varying from 4.5% in 2001 to 6.7% in 2006. Although the number of births were higher in 2003 compared to 2001 ($p = 0.002$), 2005 and 2006 ($p < 0.05$), respectively, the number of HIV-1-infected children remained unaltered over the years. Surprisingly, no vertical transmission occurred in 2005 (Figure 1).

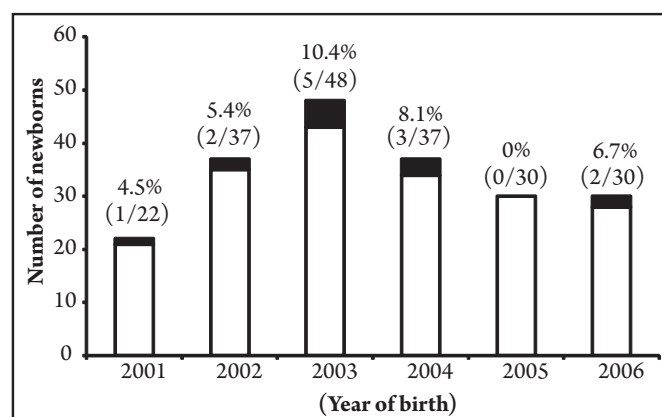


FIGURE 1 - Vertical HIV transmission rate among HIV-1-infected women attended at the DRS II in Araçatuba and at the DRS XI in Presidente Prudente, State of São Paulo. (noninfected: opened bars, infected: closed bars). DRS: Regional Health Departments.

Testing for CD4 and HIV-1 viral load in children after delivery is an important procedure to control MTCT. According to the instructions of the Brazilian Ministry of Health HIV-AIDS program, the viral load of newborns should be determined at both 2 and 4 months following delivery by HIV-1-positive mothers. The distribution throughout the period was similar in the Araçatuba and, Presidente Prudente regions. About 60% of mothers brought their babies for blood sampling within the suggested timeframe, which was no later than four months after birth. The number of mothers bringing their babies between two and four months of age was significantly higher than those who brought their babies between birth and two months of age, four and six months and six and eight months ($p < 0.001$), respectively. An average time of 3.6 months was verified. Despite this procedure, about 20% of mothers did not know the HIV-1 status of their newborns eight months after delivery (Figure 2).

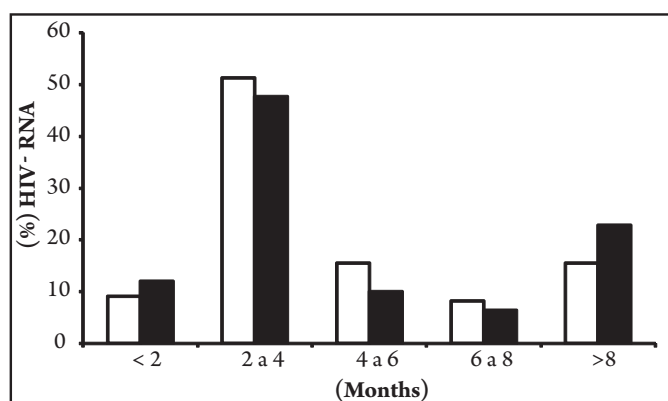


FIGURE 2 - First blood analysis of HIV-1-RNA viral load of babies born to HIV-1-infected mothers. Children referred by the DRS II (opened bars) and DRS XI (closed bars). DRS: Regional Health Departments

DISCUSSION

The global epidemic of pediatric HIV-infection reflects the epidemiology of HIV in women and the prevalence of HIV in women reflects vertical transmission in a studied population⁷. The overall prevalence rate of vertical transmission of HIV-1 in this study was 6%. This rate is similar to that verified in a nationwide multicentric study (7.1%) conducted in 2001⁸. However, it is higher than the 3.5% rate of MTCT determined for the State of São Paulo in 2002⁹. No difference was observed in the number of registered births and vertical transmission of HIV-1 in the DRS II and DRS XI. Moreover, among infected and noninfected children, no difference was verified between sexes, a result also reported in the State of São Paulo between 1983 and 1998¹⁰, and in the City of Rio Grande, Southern Brazil¹¹. The prevalence of HIV-1 in pregnant women in the region of Presidente Prudente was previously determined to be 1% of those referred to a Public Maternity hospital (PM) from 2000 to 2004¹², 0.9% of those referred to a regional university hospital from 2001 to 2005¹³ and 2.1% in women in the intrapartum period at the PM from 2005 to 2006¹⁴. These data are higher than the prevalence of 0.4% determined in a parturient sentinel study conducted by the Brazil DST/AIDS program in 2004¹⁵. Concerning vertical HIV transmission in Marília, a medium-sized city near Presidente Prudente and Araçatuba, no

children among 47 mother infant-pairs analyzed during the period from 1998 to 2000 were infected with HIV-1¹⁶. In Campinas, a HIV-1 prevalence rate of 2.9% was determined (1999-2000) and a rate of 9.7% was verified in Santos (1997-2000); these are two large cities over 300 miles from the region studied here^{3,17}. In Brazil, the prevalence of vertical HIV-1 transmission varies greatly from rates of 2.5% in the City of Campo Grande (MS)¹⁸ and 3.2% in Porto Alegre (RS)⁶ to 6.8% in Campos dos Goitacazes (RJ)¹⁹ and 21.7% in Goiania (GO)²⁰. Since vertical transmission of HIV-1 is a multifactorial and dynamic process, these results illustrate the regional and local characteristics among populations from different geographic regions. Additionally, a longer duration of antiretroviral drug use in pregnancy and special regimens of antiretroviral drugs with different protocols and time periods should be taken into account (Figure 3).

The variability in the prevalence of vertical transmission of HIV-1 throughout the period analyzed in the present study is noteworthy. Although the number of births was higher in 2003 compared to other years, the number of infected children showed no difference over the period studied. These results are contrary to the progressively decreasing values recently reported by different authors in Brazil and elsewhere^{2,3,21}. The reasons underlying these differences could be related to the organization of antenatal care. Such differences suggest a lack of standardization in the screening of HIV-1 infection and MTCT prevention. One possible explanation could be the considerable number of women who live in small municipalities that lack rigorous control measures to prevent MTCT. A nationwide program of rapid HIV testing was one of the main strategies introduced by the Brazilian STD/AIDS program to reduce the risk of MTCT^{5,22}. In the region of the DRS XI, in a regional teaching hospital, a rapid HIV-1 diagnostic test applied to pregnant women who had not been previously tested was one of the strategies applied to reduce MTCT¹³.

Determination of the HIV-1-viral status of newborns as early as possible provides an important opportunity to give medical assistance to the infants and emotional support to the mothers²³. About 60% of mothers brought their babies for both blood sampling and HIV-1 diagnosis within the suggested timeframe, which is no later than four months after birth. The peak occurred between two and four months of age, with an average time of 3.6 months.

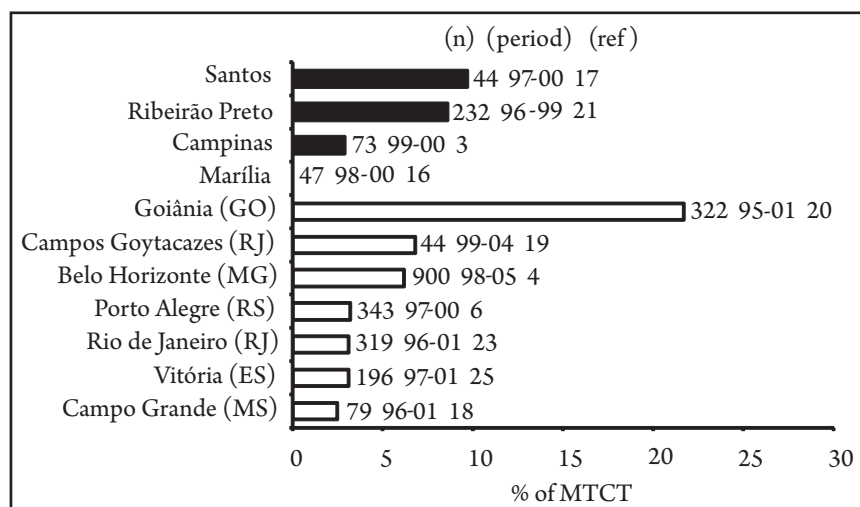


FIGURE 3 - Rates of vertical HIV-1 transmission in cities of the State of São Paulo (closed bars) and cities of Brazilian states (opened bars).

DRS: Regional Health Departments, MTCT: mother-to-child transmission.

Similarly, an average time of 4.7 months after birth was verified in the State of São Paulo for HIV-1 diagnosis, in the period from 1996 to 1998. Increased average time was reported for the States of Para (17.6) and Pernambuco (18.3) and the Federal District (18.5)¹⁰.

In spite of all the counseling given to mothers by nurses and doctors, about 40% of the women in this study did not know the HIV-status of their newborns eight months after delivery, characterizing the multifaceted aspect of the disease^{24,25}. These data suggest that new strategies should be created to motivate and convince HIV-infected mothers to determine the HIV-status of their infants, as recommended.

In conclusion, MTCT prevalence rates were similar to those obtained in a nationwide survey, but they were about 70% higher than those previously reported for the State of São Paulo.

Furthermore, a significant number of mothers did not know the HIV-status of their newborns eight months after delivery. Identifying and HIV-screening of all pregnant women in the community and performing a rapid-HIV test in women in the intrapartum period, mainly in communities with poor resources, may help to reduce regional MTCT.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

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