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# Trends in maternal-infant transmission of AIDS after antiretroviral therapy in Brazil

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## ABSTRACT

**OBJECTIVE:** the increase in the number of AIDS cases among women has led to an increase in the maternal-infant transmission of human acquired immunodeficiency virus. Measures for the control of this type of transmission were implemented in Brazil in 1996. The aim of the present study was to analyze time trends in maternal-infant transmission of AIDS among Brazilian children.

**METHODS:** The present study included children born in Brazil between 1990 and 2001. We used the database of notified AIDS cases in children 13 years of age or younger between 1990 and 2004. Exponential regression models adjusted to the time series provided the annual variation rates and observed and expected values for the period.

**RESULTS:** We found a significant increasing trend for cases born prior to the year in which antiretroviral therapy was introduced, with an increase rate of about 12% ( $t < 0.003$ ) per year. Rates from different states ranged from 5.9% to 31%. The analysis of expected and observed cases for each of the country's five Regions showed a reduction in the number of cases among children born from 1997 onwards, with a progressive year-to-year reduction. The number of notified cases among children born in 2001 was less than 10% the number of expected cases.

**CONCLUSIONS:** The results obtained suggest a favorable response the implementation of policies for the prevention of maternal-infant HIV transmission in Brazil, as observed in other parts of the world.

**KEYWORDS:** Acquired immunodeficiency syndrome, transmission. HIV. Disease transmission, vertical, statistics & numerical data. Disease transmission, vertical, prevention & control. Anti-HIV agents. Regression analysis.

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## INTRODUCTION

The patterns of dissemination of infection by the human acquired immunodeficiency virus (HIV) have changed due to the predominance of heterosexual transmission. This has been decisive for the increase in the incidence of the disease among women. In its turn, the increase in the number of cases among women led to an increase in maternal-infant transmission of HIV infection, with consequent increase in the number of cases of AIDS in children worldwide. In Brazil, about 84% of pediatric AIDS cases – that is, cases among children up to 13 years of age – is due to maternal-infant transmission.<sup>1</sup>

The probability of maternal-infant transmission of HIV infection has been calculated in a number of studies.<sup>4-6,10,11</sup> The majority of cases of transmission – roughly 65% – occur during labor and delivery, and the remaining 35% occur during intrauterine life, especially during the last weeks of pregnancy. In addition, breastfeeding represents an additional risk of 7-22%. Studies<sup>5,6,10</sup> show that a number of factors are associated with increased risk of maternal-infant transmission of HIV. Of these, major risk factors include the time between the rupture of amniotic membranes and delivery and the amount of virus in the mother's cervical-vaginal secretions and breast milk.

The results of Aids Clinical Trial Group Protocol 076 (ACTG 076), in 1994, have proven the effectiveness of zidovudine (AZT) for the reduction of maternal-infant transmission in 67.5% of cases.<sup>5</sup> Based on this evidence, in the same year, the Centers for Disease Control and Prevention (CDC) published a recommendation for the use of AZT by HIV+ women in the second and third trimesters of pregnancy and during labor, and by children during the first six weeks of life.<sup>4</sup>

Considering the growth of the epidemic in the female population, the Brazilian Ministry of Health published, in 1995, specific regulations on the prevention of maternal-infant transmission, establishing this as one of the priorities of the National Program for STD/AIDS (PN-DST/AIDS).<sup>14</sup> However, the recommendations included in this publication were only effectively implemented with their updating and inclusion in the manuals for treatment of adults and children infected with HIV, in 1997 (Ministerial Technical Decree no. 874/97\*). Appropriate conducts for antenatal and delivery care of HIV+ women are included in the "Recommendations for the Prophylaxis

of Maternal-Infant transmission of HIV and Antiretroviral Therapy of Pregnant Women," a document periodically revised by the PN-DST/AIDS.<sup>3,7,14. \*\*</sup>

As an attempt to strengthen this control measure, another strategy<sup>9</sup> for the evaluation of the use of the maternal-infant transmission prevention protocol was the inclusion of the surveillance of HIV+ mothers and exposed children as a compulsory notification event, in 2000 (Decree n. 993/2000). Recently, with the intent of implementing measures for the reduction of morbidity and mortality related to congenital syphilis and maternal-infant HIV infection, the Ministry of Health implemented the *Projeto Nascer – Maternidades*,<sup>9</sup> within the scope of the National Unified Healthcare System (Decree n. 2,104 GM, 19 November 2002).

In Brazil, the estimated number of pregnant women infected with HIV is around 16,410, i.e., 0.4% of the population of pregnant women.<sup>2</sup> The rate of maternal-infant transmission has fallen in recent years, considering the country as a whole: from 16% in 1997,<sup>13</sup> before the introduction of antiretroviral therapy, to 7% in 2002.\*\*\* A study conducted in Rio de Janeiro in 2001<sup>11</sup> showed a reduction of about 3% in maternal-infant transmission among pregnant women participating in an intervention program that followed all recommendations made by the Ministry of Health. In 2002, the *Sentinela-Parturiente* study<sup>2</sup> showed an effective coverage of the detection of HIV infection during pregnancy of about 52% for the country as a whole. Sociogeographic inequalities become patent when comparing the country's Northeast (24%) and South (71%) regions; illiterate mothers (19%) with those with schooling above the elementary level (64%); and women who gave birth in small cities (37%) with those that delivered in cities with over 500,000 inhabitants (66%).

Therefore, in order to evaluate current measures for the control and prevention of maternal-infant transmission of HIV infection, the aim of the present study was to analyze trends in cases of AIDS among Brazilian children up to age 13 years.

## METHODS

For data analysis, we used the database of notified AIDS cases among children aged 13 years or less considered as due to maternal-infant transmission, registered in the National System for Notification Events

\*Publicada no Diário Oficial da União de 4/7/97.

\*\*Programa Nacional de DST e Aids. Ministério da Saúde. Disponível em <http://www.aids.gov.br/data/Pages/LUMISFB7D5720PTBRIE.htm> [acesso em 24 abr 2006]

\*\*\*Sociedade Brasileira de Pediatria. Resultado de Estudo Multicêntrico Brasileiro. Disponível em <http://157.86.8.37/docs/taxa%20de%20transmissao%20vertical.pdf> [acesso em 24 abr 2006]

(Sistema Nacional de Agravos de Notificação – SINAN), between 1990 and April 2004.

For the time trend analysis, we considered cases occurred in the selected period, according to year of birth. In other words, we considered the cohort of cases of AIDS notified until 2004 with birth dates between 1990 and 2001. The choice of cutoff point for year of birth was due to the concern with avoiding errors due to delays in notification. According to Szwarcwald et al<sup>12</sup> (2001), about 30% of HIV-infected children are notified as cases of AIDS only in the two first years following birth.

The use of exponential regression models, adjusted to the time-series of children with birth date between 1990 and 1996 allowed us to calculate annual variation rates and to statistically test time trends. Thus, it was also possible to estimate expected values for the entire period, allowing for a comparison between the observed and expected values for children born between 1997 and 2001.

## RESULTS

We analyzed 8,703 cases of AIDS in children aged 13 years or less, notified to SINAN until April 2004. The majority of cases occurred in the Southeast (61.7%) and South (25.2%) Regions, confirming the magnitude of the problem in these Regions in relation to the number of cases of HIV infection and AIDS in the Country.<sup>3,15</sup>

Table 1 presents observed and expected cases of maternal-child transmission of AIDS for the entire country. We highlight the fact that the rate of increase in the number of cases in the period before the introduction of antiretroviral therapy was of about 12% (mean annual variation rate = 0.12,  $p=0.003$ ). For children born in 1997, the number of cases notified represented less than 34.8% of the expected cases, a phenomenon which repeats itself progressively, with observed cases representing as little as 10% of the expected number for children born in 2001.

An analysis of time trends in maternal-infant transmission by Region shows that, prior to the introduction of antiretroviral therapy, there was a yearly increase in the number of cases in all Brazilian Regions, with mean annual variation rates ranging from 5.9% to 31%. The states of São Paulo and Rio de Janeiro, both in the Southeast Region, and at the epicenter of the AIDS epidemic in Brazil, showed the smallest increase rates in countrywide (5.9 and 8.9%, respectively). On the other hand, rates in all the States of the South Region were above 20%. The state of Espírito Santo registered

**Table 1** - Observed and expected cases of AIDS in children due to maternal-infant transmission, according to year of birth. Brazil, 1990-2001.

Brazil	Observed	Expected	(Obs-Exp/Exp)*100
1990	503	551	-8.7
1991	675	626	7.8
1992	689	712	-3.2
1993	897	808	11.0
1994	906	918	-1.3
1995	1,067	1,043	2.3
1996	1,112	1,185	-6.2
1997	878	1,346	-34.8
1998	764	1,529	-50.0
1999	622	1,737	-64.2
2000	364	1,973	-81.5
2001	226	2,241	-89.9
Total	8,703	14,669	

Mean annual variation rate (1990-1996) = 0.12;  $p=0.003$

the highest mean annual variation rate among all analyzed states (31%) (Table 2).

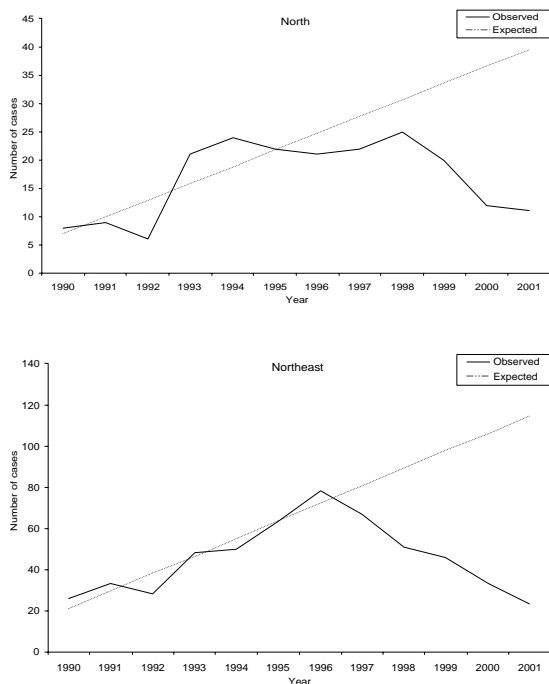
The analysis of the time series in regard to the number of observed and expected cases for each of the country's Regions shows a reduction in the number of AIDS cases notified among children born from 1997 onwards, with numbers falling progressively every year (Figure 1 and 2).

## DISCUSSION

There are still failures in the early detection of HIV among Brazilian pregnant women, as indicated by the *Sentinel-Parturiente* study.<sup>8</sup> Nonetheless, the results obtained in the present study consistently show a progressive reduction in the number of expected cases of AIDS due to maternal-infant transmission among children born from 1997 onwards. This period coincides with the massive and universal introduction of the prophylactic measures rec-

**Table 2** - Estimated mean annual variation rates in cases of maternal-child transmission of AIDS according to Region/State. Brazil, 1990-1996.

	Mean variation rate	p-value (T test)
North Region	0.23	0.01
Northeast Region	0.18	< 0.001
Bahia	0.27	0.03
Pernambuco	0.12	0.06
Southeast Region	0.12	<0.001
Espírito Santos	0.31	0.01
Rio de Janeiro	0.09	0.004
São Paulo	0.06	0.02
Minas Gerais	0.18	0.004
Midwest Region	0.24	<0.001
Paraná	0.20	< 0.001
Santa Catarina	0.26	0.01
Rio Grande do Sul	0.29	0.001
Center-West Region	0.15	0.01
Federal Distric	0.13	0.01
Goíás	0.14	0.01
Mato Grosso	0.24	<0.001
Mato Grosso do Sul	0.10	0.03
Brazil	0.12	0.003



**Figure 1** - Trends in observed and expected cases of AIDS in children due to maternal-infant transmission, according to year of birth; (a) North Region and (b) Northeast Region. Brazil, 1990-2001.

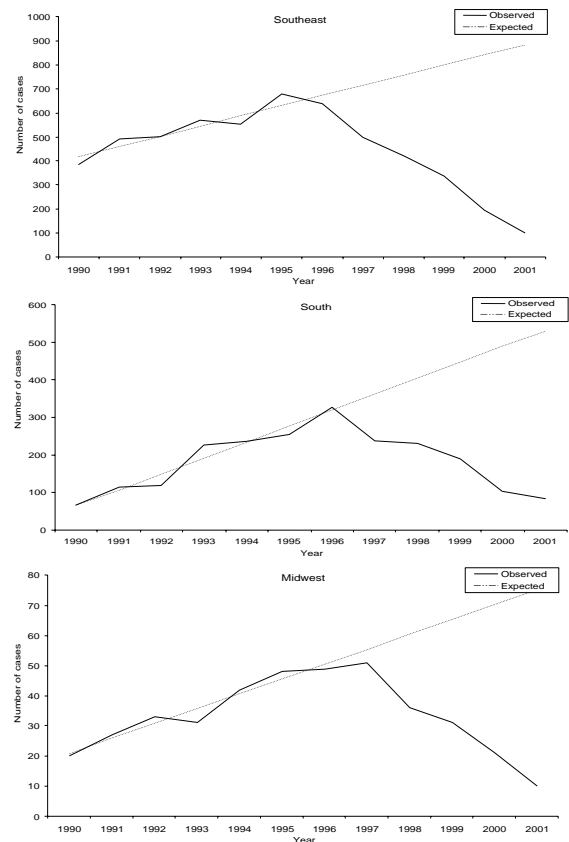
ommended by the PN-DST/AIDS, especially with regard to the administration of antiretroviral drugs to HIV+ pregnant women and to exposed newborns. The number of cases notified for children born in 2001 in the entire country represented only 10.1% of the expected number of cases. In other words, if the trend observed between 1990 and 1996 was maintained, with its 12% mean annual growth rate, a total 2,241 cases of AIDS would be expected in children born in 2001; however, only 226 cases of the disease were recorded.

The reduction in the number of expected cases occurred in all Regions. In 2001, for instance, reductions in relation to expected cases ranged from approximately 87% in the North and Northeast Regions to over 93.7% in the South Region. These differences may be partly explained by the findings of a study showing differences in access to antenatal care services between the different Regions.<sup>8</sup> In spite the reductions, the rates of maternal-infant transmission of HIV were higher in Regions with more precarious indicators of maternal care, namely the North and Northeast.\*

The reduction in the number of children with AIDS after 1997 is due to the increase in the coverage of

measures for the prevention and control of AIDS during antenatal care and delivery in Brazil, corroborating the results obtained by other authors.<sup>7,11</sup>

In conclusion, the universal adoption of antiretroviral therapy for pregnant women and children exposed to HIV has prevented around 6,000 new cases of HIV among Brazilian children born between 1997 and 2001. The results obtained by the analysis of the time series of AIDS cases due to maternal-infant transmission, according to year of birth, allowed for the identification of a decreasing trend in the number of pediatric AIDS cases, which reflects the impact of the prophylactic measures adopted in a global and efficient manner. The greater coverage of these measures, combined with greater adequacy of antenatal, delivery, and puerperal care, will surely contribute in a more rapidly effectively to the interruption of avoidable cases of maternal-infant transmission throughout the Brazilian territory.



**Figure 2** - Trends in observed and expected cases of AIDS in children due to maternal-infant transmission, according to year of birth; (c) Southeast Region, (d) South Region, and (e) Center-West Region. Brazil, 1990-2001.

\*Sociedade Brasileira de Pediatria. Resultado de Estudo Multicêntrico Brasileiro. Disponível em <http://157.86.8.37/docs/taxa%20de%20transmissao%20vertical.pdf> [acesso em 24 abr 2006]

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