

## Mother-to-child transmission of HIV: risk factors and missed opportunities for prevention among pregnant women attending health services in Goiânia, Goiás State, Brazil

Transmissão vertical do HIV: fatores associados e perdas de oportunidades de intervenção em gestantes atendidas em Goiânia, Goiás, Brasil

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### Abstract

*The objectives of this study were to estimate the risk of vertical HIV transmission and assess the associated factors and missed opportunities for prevention in a cohort of HIV+ pregnant women (1995-2001) treated in Goiânia, Goiás, Brazil, with follow-up of their children until 2005. Three data sources were compared: Information System on Reportable Diseases (SINAN), Information System on HIV+ Pregnant Women and Exposed Children (SISGHIV), and patient clinical charts. The study estimated the vertical transmission rates, factors associated with vertical transmission, and use of antiretroviral therapy. 276 HIV+ women were identified (322 pregnancies), and there were 70 HIV+ children. Overall risk of vertical HIV transmission was 27.8%. The vertical transmission rate was 40.8% in the group without prophylaxis and 1% in the group with adequate prophylaxis, i.e., a 97.5% reduction in transmission risk. Year of delivery, consultation with a specialist, and no history of injecting drug use were factors associated with adequate use of antiretroviral therapy. The study showed an important reduction in the risk of vertical transmission in pregnant women who received adequate therapy, besides identifying missed opportunities for prevention.*

*Vertical Disease Transmission; HIV; Pregnancy*

### Introduction

Vertical transmission or mother-to-child transmission, is the main source of the HIV infection in children, and it may occur before, during, or after birth. In 1994, the results of a clinical trial by the AIDS Clinical Trial Group (ACTG-076) were made available, which is considered a landmark in the prevention of vertical HIV transmission <sup>1</sup>. The strategies for reducing the risk of transmission include serological anti-HIV screening during prenatal, the use of antiretrovirals to reduce maternal viral load during gestation and delivery, elective caesarean section, proscriptio of breastfeeding, and the use of antiretrovirals during the newborns first six weeks of life <sup>2,3</sup>. The implementation of these preventive measures has determined an important reduction in vertical transmission rates, particularly in developed countries, in the last ten years <sup>4,5,6</sup>. In 2001, the Joint United Nations Programme on HIV/AIDS (UNAIDS) set a goal of a global reduction from 20% and of 50% in the number of children infected with HIV in the years 2005 and 2010, respectively <sup>6,7</sup>. In some developed countries it has been possible to achieve an even greater reduction than that proposed, with rates of vertical transmission ranging from 1 and 8% in the post ACGT-076 era <sup>6,8,9</sup>. Meanwhile, estimates from the World Health Organization (WHO) pointed to 700,000 new infections among children in non-industrialized countries in 2003, principally in Sub-Saharan Africa <sup>7</sup>.

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In Brazil, vertical transmission was responsible for around 85% of AIDS cases in children from 1994 to 2005<sup>10</sup>, and reduction of vertical transmission has been among the priorities of the Brazilian National STD/AIDS Program (PNDST/AIDS) of the Brazilian Ministry of Health. Prenatal screening for HIV as well as free prophylactic medication for pregnant women and their babies were implemented in Brazil in 1995. At the end of the 1990s, it was estimated that there had been approximately 15,000 deliveries from HIV infected women, although only about 20% of them had received treatment<sup>11</sup>. Even with the increase in prophylactic action coverage in recent years, the PNDST/AIDS has estimated that only 35% of HIV positive pregnant women had access to antiretroviral therapy in 2001<sup>12</sup>. A sentinel study of women in labor in 2002, gave evidence of only a 52% effective coverage for HIV testing during pregnancy, with known socio-spatial inequalities in Brazil<sup>13</sup>. The spread of the epidemic in the female population of low income and education, has been aggravated by the inadequate prenatal healthcare and the subsequent risk of vertical HIV transmission<sup>14,15</sup>. In the Central Western Region, an analysis of the AIDS epidemic in the 1990s showed an “interiorization” and “feminization” of the epidemic<sup>16</sup>, characterized by an increase in the number of cases of mother-to-child transmission in the region.

In the pre- ACTG-076 period, it is estimated that there was a 16% to 20% vertical HIV transmission rate in São Paulo, Brazil. After the implementation of the prevention measures by the Brazilian Ministry of Health, the rates of vertical transmission have varied between 2.5% and 8.6% in Brazil<sup>17,18,19,20,21,22,23</sup>. These estimates were obtained predominantly from reference centers in the Southeastern Region, and do not necessarily reflect the existing conditions in the majority of healthcare services. Considering the diversities of the HIV/AIDS epidemic in our country, it is important to evaluate vertical HIV transmission, at healthcare services, in other Brazilian regions. In addition, it is fundamental to identify factors that interfere with achieving the stipulated goals for reduction of mother-to-child transmission.

This study aims to estimate vertical HIV transmission risk and evaluate the factors associated with the use of antiretrovirals for prevention of vertical HIV transmission in women followed in healthcare services of reference in the city of Goiânia, Goiás, Brazil. It is interesting to establish a baseline, between 1995 and 2001, assessing both maternal characteristics and those of the healthcare services responsible for the preven-

tative measures, with the goal of implementing future actions to reduce vertical transmission.

## Methods

This is an ambi-directional cohort study, including HIV-positive women with at least one pregnancy between 1995 and 2001, followed by public healthcare services of reference for HIV/AIDS in Goiânia. The children exposed to HIV were monitored for a minimum of 18 months after birth, with a final serology status review done in September 2005.

The Hospital de Doenças Tropicais Dr. Anuar Auad [Dr. Anuar Auad Tropical Disease Hospital] and the Hospital Materno Infantil [Maternal and Children's Hospital], both pertaining to the Goiás State Health, were selected as places for the search, identification, and investigation of cases of pregnant women with HIV/AIDS exposed concepts. The Hospital de Doenças Tropicais Dr. Anuar Auad was responsible for treating around 90% of AIDS cases from 1984 to 2001 and the Hospital Materno Infantil for around 80% of the deliveries for HIV/AIDS reported for women in Goiás, according to the Reportable Diseases Database (SINAN) and the Database on HIV+ Pregnant Women and Exposed Children (SIGSHIV). Reviews of 1,095 medical records of HIV-infected women were done to identify those who had had at least one pregnancy, as well as their respective children, at the reference hospitals, between 1995 and 2001.

A databank was created, using the mother's name to link the maternal and pediatric records from the Hospital de Doenças Tropicais Dr. Anuar Auad, and obstetric records from the Hospital Materno Infantil, and the registers of SINAN and SIGSHIV. There were 276 HIV-infected women identified who had had at least one pregnancy during the period. A structured questionnaire for data extraction was created, including: sociodemographic characteristics, exposure category, clinical and laboratorial records, obstetric history, and use of antiretroviral prophylaxis, as established by the PNDST/AIDS 2003<sup>2</sup>.

The diagnostic criteria for HIV/AIDS infection in women and children were established in accordance to Brazilian Ministry of Health guidelines for epidemiological surveillance purposes<sup>24,25</sup>. A child was considered infected when tested positive for RNA-HIV through a polymerase chain reaction (PCR) in two samples. In children 18 months or older, the diagnosis of the infection was carried out through detection of anti-HIV antibodies using the Elisa technique (two tests), followed by a confirmation test using the Western-

blot technique. Criteria adopted for the exclusion of the HIV infection were: two negative samples for RNA-PCR (minimum age of two months), at least one of them done after the fourth month of life; negative results of two anti-HIV serology exams with an interval of at least one month between them for children less than 18 months old; for children 18 months or older the negative results for an anti-HIV antibodies, according to guidelines from the Brazilian Ministry of Health <sup>2,25</sup>. The inconclusive category included loss to follow-up and neonatal deaths. Children with negative serological tests or with negative RNA-PCR results not obtained at appropriate scheduled time were considered to be probably uninfected.

The criteria of the Brazilian Ministry of Health for the prophylaxis of vertical transmission during pregnancy and delivery, and after birth, were also adopted <sup>2</sup>. The use of antiretrovirals for prevention of vertical HIV transmission in this study were classified as: adequate – use during pregnancy, delivery, and for the newborn up to the sixth week of life; partial – use during one or two phases or for an inadequate period; absent – no antiretroviral use in any of the three phases. Quantification of HIV maternal viral load was classified, for analysis, as detectable or undetectable. The CD4 cell counts were categorized as  $> 350$  or  $\leq 350$  cells/mm<sup>3</sup>. Results of HIV viral load and CD4 counts obtained up to six months after birth were included. For cases with more than one laboratory result, the result obtained nearest the time of birth was included.

#### Data analysis

A descriptive analysis of the main sociodemographic characteristics of the mothers and children was carried out. In the case of a twin pregnancy, information from one of the babies was considered. Measures of central tendency and dispersion were calculated for continuous variables and frequencies were calculated for categorical variable. Chi-square or  $\chi^2$  tests for trend were used, to evaluate differences of proportion with statistical significance of 5% ( $p < 0.05$ ). The percentage of vertical HIV transmission was estimated with a respective 95% confidence interval (95%CI), having as a numerator the number of children infected, and as a denominator the number of exposed children. The reduction of risk among the mother-child pairs without prophylaxis versus pairs with adequate prophylaxis was also calculated.

Univariate analysis was carried out to evaluate factors associated with the adequate use of antiretrovirals for the prevention of vertical HIV

transmission in women who had been diagnosed with the infection before delivery. Also evaluated were factors associated with vertical HIV transmission. The odds ratio (OR) was estimated with the respective 95%CI among exposure variables and outcomes. A correlation matrix and Pearson's test were carried out to select the variables included in the multivariate logistic regression model <sup>26</sup>. The programs Epi Info 6.0 (Centers for Disease Control and Prevention, Atlanta, U.S.A.) and SPSS version 10.0 (SPSS Inc. Chicago, U.S.A.) were used.

The study was approved by the Ethical Institutional Review Board.

#### **Results**

There were 276 women living with HIV/AIDS with at least one pregnancy between 1995 and 2001, followed in Goiânia. Of these, 83.8% (231/276) had one gestation, and two of these had twins. There were 44 (15.9%) women who had two gestations, and one with three, for a total of 322 gestations and 324 babies, in the period studied. The official databases (SIGHIV and SINAN) showed records for 99 mother-child pairs, corresponding to 30.7% of the cases studied.

Approximately 60% of the women were residents of the city of Goiânia or its surroundings. All reported sexual relations as a transmission factor and 8.6% also cited intravenous drug use as potential exposure category. Among those who gave information about educational level, 82.4% had less equivalent to 8 years of schooling. However, for 40.2% of women information about educational level was not available. The majority did not have any income, 64% were in the housewife category, and 7.3% were students. Among the 64 women with a source of income, 53 did unskilled work, 6 were sex workers, and 5 were health professionals. The maternal age at the time of delivery, varied from 14 to 44 years, with an average of 25 years (SD = 5.0 years), with prenatal recorded in 202 gestations. Of a total of 322 deliveries, 38.5% were vaginal deliveries, and 42.4% were caesarean section. The diagnosis of HIV infection was made before gestation in 76 (23.6%) women, during pregnancy or delivery in 94 (29.2%), and after delivery in 152 (47.2%) women. Eighty-seven women (27.1%) had AIDS, of whom eleven had an opportunistic disease during gestation. Table 1 shows the main socio-demographic characteristics of the 276 women at the time of their first HIV positive pregnancy. It also presents the obstetric characteristics of 322 pregnancies that occurred between 1995 and 2001 in women with HIV/AIDS, followed up in Goiânia.

There were 318 live births, one abortion, one fetal death, and two stillbirths recorded. Among the live births, five died during the neonatal period and 28 succumbed to opportunistic diseases. In relation to gestational age, 246 of the newborns were full term babies, and 21 premature babies. Low birth weight was recorded in 11% of the newborns. Follow-up at the reference facility was recorded in 89% of the 318 live births, and the majority of children (70%) had the first follow-up visit at the reference center after 30 days of life. Breastfeeding was recorded in 100 children, 66 of them for more than 30 days.

There were 70 children diagnosed HIV seropositive and 182 seronegative. Of the 66 children with undefined infectious status, according to the criteria of the Brazilian Ministry of Health, 29 were classified as probably uninfected. Of the remaining 37 children whose infectious status was not known, 5 died during neonatal period and 32 were lost to follow-up. Thus, of the 318 children evaluated, 11.6% had an inconclusive diagnosis for HIV infection.

The risk for mother-child transmission was estimated at 27.8% (95%CI: 22.3-33.7). The lowest and highest estimates of transmission risk, assuming that all children with undefined serological status were uninfected or that all were infected, were, respectively, 22% (95%CI: 17.6-36.9) and 42.2% (95%CI: 37.3-48.9). The risk of mother-child transmission was greater (40.8%; 62/152) among women who were diagnosed with HIV after delivery, compared with the women with a pre-delivery diagnosis (4.8%; 8/166), a significant statistical difference ( $\chi^2 = 56.2$ ;  $p < 0.001$ ). The proportion of those infected was 52% in the period from 1995-1997 and 29.3% from 1998-2001. In 147 (95.7%) of the 152 women with post-delivery diagnosis, there had been HIV/AIDS recorded in a family member (partner, mother and/or her baby), suggesting late maternal diagnosis.

Figure 1 shows the number of children according to their serological status and the percentage of maternal pre-delivery HIV diagnoses during the period from 1995-2001. The number of births varied from 39 to 61 children per year. There was a reduction in the proportion of HIV positive children between 1995 and 2001 ( $\chi^2 = 4.44$ ; 6df;  $p = 0.035$ ) and an increase in the proportion of pre-delivery diagnoses between 1995 and 2001 ( $\chi^2 = 53.0$ ; 6df,  $p < 0.01$ ).

Diagnosis of the children in relation to HIV infection, stratified by time of maternal diagnosis and use of antiretrovirals for prophylaxis of vertical transmission, is presented in Figure 2. Among the 166 women with HIV diagnosis before delivery, 96 pairs of mother and babies received adequate antiretroviral prophylaxis, that is, dur-

Table 1

Profile of HIV-infected pregnant women under follow-up in Goiânia, Goiás, Brazil, from 1995 to 2001.

Variables	Total	
	n	%
Sociodemographic characteristics (N = 276 women)		
City of residence		
Goiânia	177	64.1
Other	99	35.9
Education (years)		
≤ 8	136	49.3
> 8	29	10.5
Ignored	111	40.2
Marital status		
Stable sexual partner	189	68.5
No stable sexual partner	75	27.2
Ignored	12	4.3
Exposure category		
Sexual	244	88.4
Sexual/Injection drug use	23	8.3
Ignored	9	3.3
Obstetric characteristics (N = 322 pregnancies)		
Number of gestations		
One	231	83.8
Two	44	15.9
Three	1	0.3
Age at delivery (years)		
≤ 20	39	12.1
> 20	269	83.6
Ignored	14	4.3
Prenatal care		
Yes	202	62.7
No	13	4.1
Ignored	107	33.2
Type of delivery		
Vaginal	124	38.5
Caesarean	136	42.2
Ignored	62	19.3
Time of diagnosis		
Before gestation	76	23.6
During gestation/Delivery	94	29.2
After delivery	152	47.2
AIDS		
Yes	87	27.1
No	231	71.7
Ignored	4	1.2

ing gestation, delivery, and during the first six weeks of life for the newly born; 52 pairs received a partial regimen, and 18 did not receive antiretrovirals at any phase. There were 152 women who were diagnosed with the HIV infection after

Figure 1

Number of children according to the infection status and maternal pre-delivery diagnostic percentage, in relation to the year of birth.

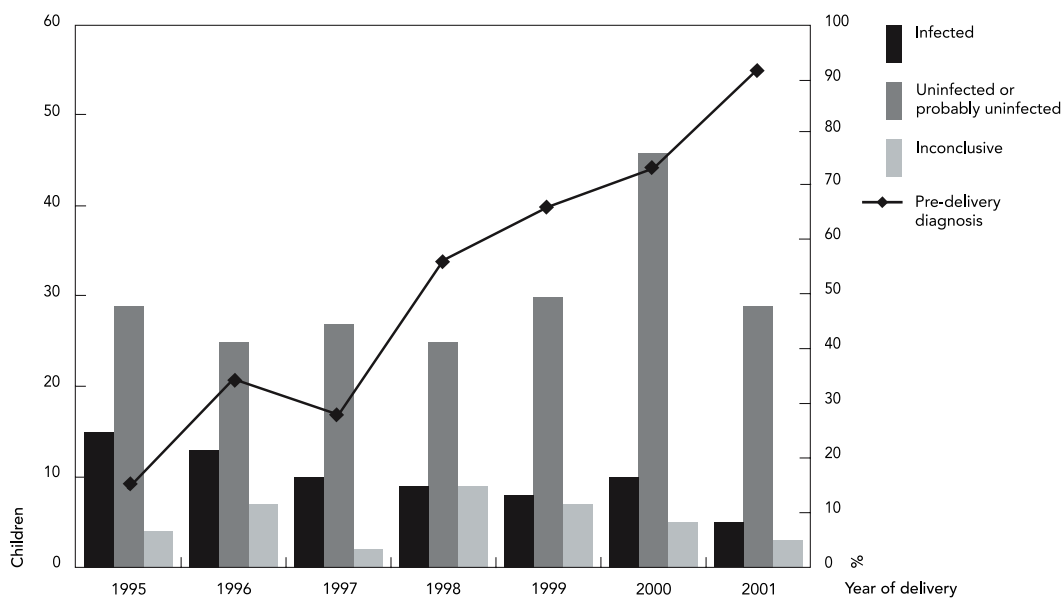
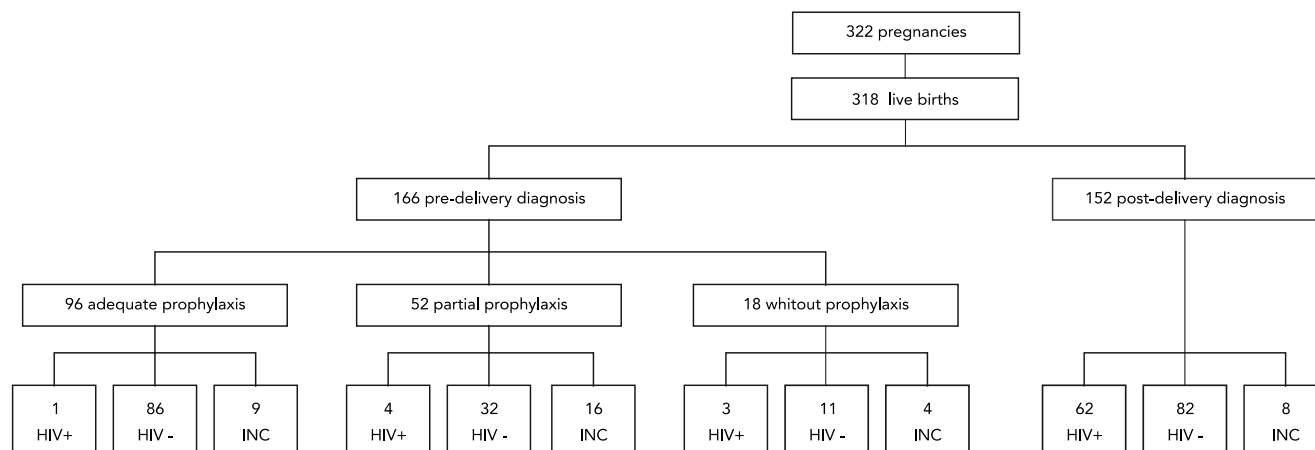


Figure 2

Infections status of the children in relation to time of maternal diagnosis and use of antiretrovirals.



HIV+: infected children; HIV-: uninfected children or probably uninfected; INC: inconclusive.

delivery, and none of them had received antiretrovirals during pregnancy or delivery.

During pregnancy and/or delivery, 123 women used some type of antiretroviral medication. Of these 27.6% (34/123) had already been using antiretrovirals before gestation: 53% (18/34) used a triple scheme with protease inhibitor; 8.8% used a triple scheme without protease inhibitor; and 38.2% (13/34) used a double scheme. For the 189 women who began antiretroviral use during gestation: 61 received AZT (Zidovudine); and 28 received schemes with two or three antiretroviral drugs. Regular use of antiretrovirals during gestation was reported in 82.9% (102/123) of the pregnant mothers.

During delivery injectable AZT was administered to 112 of 166 gestating women who had had a pre-delivery HIV diagnosis. There were 38 pregnant women who did not receive prophylaxis in this stage, and it was not possible to identify motives for not having used this drug during these deliveries. For 24 of the pregnant women the place of the delivery was known, which in 21 cases took place in maternities of the public health network of Goiânia, and of which 28.6% (6/21) took place after 1999. AZT syrup was prescribed to 130 newborns, of whom 126 received this intervention during the first 12 hours of life. There were 36 newborns who did not receive AZT, and the motives identified for not giving it to twenty children were: no offer/prescription at healthcare service in 14 cases; and maternal refusal in six cases.

An increase was noted in the proportion of correct use of prophylaxis (during pregnancy, delivery, and post-delivery) between 1995 and 2001 ( $\chi^2 = 31.9$ ; 6df;  $p < 0.01$ ). In the group of pregnant women and newborns who received adequate therapy, the risk of vertical transmission was 1% (95%CI: 0.02-5.7). For the group of pregnant women and newborns who had incomplete or no usage of antiretrovirals, this percentage was 7.4% (95%CI: 2.4-18.7). A 97.5% reduction occurred in vertical transmission rates, if comparing the group that received prophylaxis in all three phases with the one that did not receive any antiretrovirals in any phase (1% versus 40.8%).

Factors related to the adequate use of antiretroviral schemes for the prevention of vertical transmission were analyzed for 157 women from a total of 166 with pre-delivery diagnosed HIV. In univariate analysis the following factors were associated with inadequate use of antiretrovirals: "year of birth", "place of delivery", "not cared for by specialist", "use of injection drugs", and "no fixed sexual partner" (Table 2). The variable "place of delivery", although associated with the

adequate use of prophylaxis in univariate analysis, was not included in the multivariate model because of its correlation with the variable "cared for by a specialist". In multivariate regression logistic analysis, variables independently associated with inadequate antiretroviral prophylaxis were: year of birth between 1995 to 1997 (OR adjusted = 21.9; 95%CI: 7.0-60.0), "not cared for by specialist" (OR adjusted = 19.4; 95%CI: 5.5-68.0), and "use of injection drugs" (OR adjusted = 5.9; 95%CI: 1.2-28.6).

To analyze the factors possibly related to vertical HIV transmission, 252 pairs of mothers and children were included who had been defined as having, or not having, HIV infection. The following factors were shown in a univariate analysis to be associated with HIV transmission risk: year of birth, place of residence, vaginal delivery, not having had a pediatric consultation during the first 30 days of life, breastfeeding, and not having received antiretrovirals during gestation, delivery or the first six weeks of life (Table 3). There was colinearity shown among the variables: use of antiretrovirals, breastfeeding, type of delivery, year of birth, and pediatric consultation during the first days of life ( $p < 0.01$ ).

## Discussion

In this study, the percentages of vertical HIV transmission and risk factors associated with the use of antiretrovirals in the city of Goiânia when preventive measures for vertical transmission were already available free of charge in the public health system where analyzed, starting in 1995. Health services selected for identifying the pairs of HIV-infected mothers and exposed children were responsible for the attendance of almost all the reported cases in the state, indicating the representative casuistic studied<sup>27</sup>. Approximately 35% of HIV/AIDS infected pregnant women treated in Goiânia were from other cities, suggesting that the treatment outside the capital may be inadequate. Pregnant who lived outside the capital also had higher risk of vertical HIV transmission, reinforcing the hypothesis of a differentiation in the availability of prophylactic measures, according to the place of residence. This situation is compatible with inequalities in access to preventative actions reported in other regions of Brazil<sup>13,28,29</sup>.

The strategy adopted in this study of identifying HIV-infected pregnant women and their babies in the main health services of Goiânia, with linkage to the data from the official systems (SINAN and SISGHIV), enabled an increase from 99 to 322 mother-child pairs evaluated. This is

Table 2

Factors associated with antiretroviral use to prevent vertical HIV transmission in 157 gestating women under follow up in Goiânia, Goiás, Brazil, from 1995 to 2001.

Variables *	Inadequate (n = 61)	Adequate (n = 96)	OR (95%CI)	p
Characteristics of healthcare service				
City of residence				
Goiânia	41	69	1.0	
Other	20	27	1.3 (0.6-2.6)	0.53
Year of delivery				
1998-2001	33	91	1.0	
1995-1997	28	5	15.4 (5.2-54.4)	< 0.01
Delivery in reference facility				
Yes	27	88	1.0	
No	8	3	8.7 (1.9-44.9)	< 0.01
Consultation with specialist				
Yes	37	92	1.0	
No	24	4	14.9 (4.5-54.8)	< 0.01
Maternal characteristics				
Age at delivery (years)				
≥ 20	49	87	1.0	
< 20	10	9	1.9 (0.7-5.7)	0.162
Exposure category				
Sexual	49	93	1.0	
Sexual + IDU	12	3	7.6 (1.9-35.7)	< 0.01
Children before present gestation				
≤ 1	59	90	1.0	
> 1	1	5	0.3 (0.1-2.8)	0.25
AIDS before or during gestation				
No	38	58	1.0	
Yes	23	38	0.9 (0.5-1.9)	0.81
Stable partner				
Yes	38	74	1.0	
No	21	22	1.9 (0.9-4.0)	0.09

IDU: injection drug user.

\* Numbers do not always add up to total because of missing data.

compatible with under-notification rates of 15% to 70% for AIDS cases, reported in various geographic regions of Brazil<sup>30,31</sup>. In the present study, 12.7% of HIV infected pregnant women were adolescents, some of them, with less than 15 years old. Considering education as an indicator of socioeconomic conditions, the majority of these women only had elementary education. This information needs to be analyzed with caution, as there was no register of education for 40% of this population. Poor education and inaccurate recording of this variable are in agreement with the sociodemographic characteristics of the AIDS epidemic in Brazil<sup>14,16</sup>. The majority of pregnant women included did not have their

own source of income or did unskilled work, and this was also observed among HIV-positive pregnant women cared for at a university hospital in the city of Rio de Janeiro<sup>19</sup>. A potential selection bias could occur if women with a higher socioeconomic level do not use public health services, and are therefore not recorded. These data reinforce the importance of properly recording information to establish vulnerability profiles, enabling prevention strategies to be directed to a young and poorly-educated population.

In this study, the percentage of vertical HIV transmission was 4.8% among pregnant women with a diagnosis previous to delivery. This result was similar to those obtained in other cities, es-

Table 3

Univariate analysis of factors associated with vertical HIV transmission in 252 pregnant women followed up in Goiânia, Goiás, Brazil, from 1995 to 2001.

Variables *	HIV+ (n = 70)	HIV- (n = 182)	OR (95%CI)	p
Maternal characteristics				
Clinical situation of mother at delivery				
HIV carrier	54	134	1.0	
AIDS	14	47	0.7 (0.4-1.5)	0.38
Maternal viral load (copies)				
Undetectable	1	20	1.0	
Detectable	4	57	1.4 (0.1-35.0)	0.77
Maternal CD4 count (cells/mm <sup>3</sup> )				
> 350	3	59	1.0	
≤ 350	5	26	3.8 (0.7-22.0)	0.07
Maternal breastfeeding				
No	11	99	1.0	
Yes	38	55	6.2 (2.8-14.1)	< 0.01
Characteristics of health service				
Residence in Goiânia				
Yes	31	125	1.0	
No	36	56	2.6 (1.4-4.8)	< 0.01
Year of delivery				
1998 to 2001	32	109	1.0	
1995 to 1997	38	73	1.8 (1.0-3.2)	< 0.05
Type of delivery				
Caesarean	20	89	1.0	
Vaginal	33	64	2.3 (1.1-4.6)	< 0.01
Pediatric consultation				
First 30 days of life	3	68	1.0	
After 30 days of life	67	108	11.5 (3.3-48.1)	< 0.01
Antiretroviral use during gestation				
Yes	4	82	1.0	
No	66	100	11.9 (3.9-40.5)	< 0.01
Injectable AZT during delivery				
Yes	2	80	1.0	
No	66	95	27.8 (6.4-169.4)	< 0.01
AZT syrup for the newborn				
Yes	3	95	1.0	
No	67	84	25.3 (7.3-104.6)	< 0.01
Antiretroviral prophylaxis				
Adequate/Partial	5	100	1.0	
Absent	65	82	15.8 (5.8-47.0)	<0.01

\* Numbers do not always add up to total because of missing data.

pecially in the Southeastern Region <sup>19,20,23</sup>. Nevertheless, in 47% of the pregnant HIV-infected women there was late diagnosis of the infection, with a risk of vertical transmission eight times greater (40.8%), comparable to transmission estimates of the pre ACTG-076 era <sup>6</sup>. In Brazil the estimated risk of vertical transmission before the

implementation of preventive measures was 16% in a cohort of pregnant women in São Paulo <sup>17</sup>. In this cohort the percentage of mothers with AIDS or who breastfed their babies was lower than in the present study, which may account in part for the high percentage of vertical transmission found among women in the present study



who did not receive antiretroviral prophylaxis. It is also possible that there was an overestimate of vertical transmission in the present study, as the cases were identified at HIV/AIDS centers.

This study demonstrated a reduction in vertical transmission risk of 97.5%, measured in routine public healthcare services, when comparing mother-child pairs who received adequate prophylaxis during the three stages (1%) with those pairs that had no intervention (40.8%). Nevertheless, almost half the HIV/AIDS pregnant women were diagnosed with the infection after delivery, indicating important loss of opportunities for prevention of vertical transmission. During the study period (1995-2001) a significant reduction in the proportion of late diagnoses (post-delivery) was observed, signaling that there had been an improvement in the offer of HIV screening tests, with a resulting reduction in the numbers of children infected in recent years. The results of this study were compatible with national estimates of low HIV testing coverage, and of low access to antiretroviral therapies by pregnant women<sup>13,32</sup>.

Among the factors associated with high vertical transmission risk, this study identified, in univariate analysis, major risks for infection among children delivered vaginally and/or breastfed. At the end of the 1990s, the result of a meta-analysis gave evidence that elective caesarean section reduced the risk of vertical HIV transmission by more than 50%<sup>33</sup>. The additional risk for vertical HIV transmission through breastfeeding is described as between 7% and 22%<sup>34,35</sup>. Recent studies document an additional risk of vertical HIV transmission of 16%, after a child is breastfed for two years<sup>6</sup>. However, in the present study the mode of delivery and breastfeeding were associated with the use of antiretrovirals. The majority of women who receive antiretrovirals do not breastfeed their babies, while the majority of women not receiving antiretrovirals do breastfeed their babies. Mode of delivery, maternal breastfeeding, and use of antiretrovirals present high degree of colinearity, suggesting that know-

ing or not knowing the serological status of the gestating woman defines one of two paths: (a) use of antiretrovirals and no breastfeeding or (b) no use of antiretrovirals and breastfeeding. Therefore it can be inferred that the choice of a path depends on carrying out a pre-delivery HIV screening test, making possible access to preventative measures.

In accordance with the results of this study, biological markers indicating the progress or inadequate control of the HIV infection, such as detectable viremia and low CD4 counts were not associated with higher risks of vertical transmission, differing from other studies<sup>36,37</sup>. Among the possible limitations, we should mention: small sample size, the cut-offs utilized (detectable or undetectable viremia, CD4 < or  $\geq$  350), with low discriminatory power and the varying time of assessment of these biological markers in relation to delivery. The percentage of premature births (7.1%) in this cohort of newborns from HIV-positive mothers did not differ from the values described for the total of live births in Goiânia during the period from 1990 to 2000<sup>38</sup>. Meanwhile the indices of perinatal and infantile death were greater than those values estimated for Goiânia<sup>39</sup>. Intrauterine HIV infection, compromised maternal health, adverse effects of antiretroviral drugs, as well as socioeconomic factors may contribute to this unfavorable precocious evolution, among children and HIV-positive mothers.

These results demonstrate the importance of early diagnosis as the first strategy, which makes possible the determination of adequate conducts for the protection of children exposed to HIV. It emphasizes the importance of routine HIV screening during the prenatal, and the necessity of ensuring the implementation of those practices recommended by the Brazilian Ministry of Health, to guarantee prevention. This study also points out the necessity for training health professionals throughout the state and implementing strategies directed to the more vulnerable groups, who are poorly educated adolescents with unfavorable socioeconomic conditions.

## Resumo

Os objetivos foram estimar o risco de transmissão vertical do HIV e avaliar fatores associados e perdas de oportunidades de prevenção em coorte de gestantes HIV+ (1995-2001), atendidas em Goiânia, Goiás, Brasil, com seguimento das crianças até 2005. Foi realizada conciliação de três fontes de dados: Sistema de Informação de Agravos de Notificação (SINAN), Sistema de Informação de Gestantes HIV Positivas e Crianças Expostas (SISGHIV) e prontuários médicos. Foram estimados os percentuais de transmissão vertical, fatores associados à transmissão vertical e ao uso de terapia anti-retroviral. Foram identificadas 276 mulheres HIV+ (322 gestações) e os desfechos foram 70 crianças HIV+. O risco de transmissão vertical do HIV foi de 27,8%. A transmissão vertical foi de 40,8% no grupo sem profilaxia e de 1% no grupo com profilaxia adequada, com 97,5% de redução do risco de transmissão. Ano do parto, consulta com especialista e não ter antecedentes de drogas injetáveis foram fatores associados ao uso adequado de terapia anti-retroviral. O estudo evidenciou importante redução do risco de transmissão vertical em gestantes que receberam terapia adequada e identificou oportunidades perdidas para prevenção.

*Transmissão Vertical de Doença; HIV; Gravidez*

## Contributors

M. D. Turchi was responsible the study design, data analysis, and writing and editing the manuscript. L. S. Duarte participated in all stages of the project and was responsible for data collection. C. M. T. Martelli contributed to the data analysis stage and the final version of the manuscript.

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