Article/Artigo

Mother-to-child transmission of HIV infection in Manaus, State of Amazonas, Brazil

Transmissão materno-infantil da infecção pelo HIV em Manaus, Amazonas, Brasil

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ABSTRACT

Introduction: Reduction in the vertical transmission of HIV is possible when prophylactic measures are implemented. Our objective was to determine demographic characteristics of HIV-infected pregnant women and the rate of mother-to-child transmission of HIV in Manaus, Amazonas, Brazil. **Methods**: A descriptive study was conducted using notification, and investigating data from the Notifiable Diseases Data System in the Brazilian State of Amazonas, between 2007 and 2009. **Results**: During the study period, notification was received of 509 HIV-positive pregnant women. The vertical transmission was 9.9% (95% CI: 7.2-12.6%). The mean age of women was 27 years (SD: 5.7), and the majority (54.8%) had not completed elementary school (eighth grade). Diagnosis of HIV seropositivity was made prior to pregnancy in 115 (22.6%) women, during prenatal care in 302 (59.3%), during delivery in 70 (13.8%), and following delivery in 22 (4.3%). Four hundred four of these women (79.4%) had had prenatal care, with 79.4% of patients receiving antiretroviral during pregnancy and 61.9% of the newborn infants receiving prophylaxis. In the final multivariate logistic regression model, living in urban area [OR = 0.7 (95% CI: 0.35-0.89)] and having had prenatal care [OR = 0.1 (95% CI: 0.04-0.24)] remained as protective factors against vertical HIV transmission in this population. **Conclusions**: The relevance of adequate compliance with the measures already established as being effective in guaranteeing a reduction in HIV transmission within the maternal and infant population should be emphasized.

Keywords: Vertical transmission. HIV. AIDS. Pregnancy. Prophylaxis.

RESUMO

Introdução: A redução da transmissão vertical do HIV é possível quando medidas profiláticas são implementadas. Nosso objetivo foi determinar as características demográficas de gestantes soropositivas e a taxa de transmissão vertical do HIV em Manaus, Amazonas, Brasil. **Métodos**: Estudo descritivo foi realizado usando dados de notificação e investigação do Sistema de Informações de Agravos de Notificações (SINAN) do Estado do Amazonas e pesquisa de informações em prontuários das gestantes na Maternidades do Município de Manaus, entre 2007 e 2009. **Resultados**: No período do estudo, foram notificadas 509 gestantes HIV positivas. A taxa de transmissão vertical foi de 9,9% (95%CI: 7.2 - 12.6%). A idade media das pacientes era de 27 anos (SD: 5,7) e a maioria (54,8%) não completou o ensino fundamental. O diagnóstico da infecção pelo HIV foi realizado antes da gravidez em 115 (22,6%) pacientes, durante o pré-natal em 302 (59,3%), no momento do parto em 70 (13,8%) e no puerpério em 22 (4,3%). Quatrocentos e quatro (79,4%) gestantes tiveram acompanhamento pré-natal, com (79,4%) das pacientes recebendo drogas antirretrovirais na gestação e 61,9% dos recém-nascidos recebeu profilaxia antirretroviral. No modelo final de regressão logística multivariada, residir em área urbana [OR=0,7 (95%CI: 0,35-0,89)] e ter realizado pré-natal [OR=0,1 (95%CI: 0,04-0,24)] demonstraram ser fatores protetores da transmissão vertical nesta população. **Conclusões**: A relevância de acompanhamento adequado e instituição de medidas já estabelecidas como efetivas em garantir a redução da transmissão vertical do HIV em gestantes e seus recém-nascidos deve ser enfatizada.

Palavras-chaves: Transmissão vertical. HIV. AIDS. Gravidez. Profilaxia.

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INTRODUCTION

The majority of HIV-positive women are young and of reproductive age[1]. The increase in the heterosexual form of transmission was an important factor in increasing the incidence of AIDS cases in women and, consequently, in increasing the number of AIDS cases in children as a result of vertical HIV transmission[2].

A considerable percentage of the cases of HIV infection in the female population are diagnosed during pregnancy, reflecting the appropriateness of prenatal health-care policies requiring serological screening for HIV[3]. The estimated prevalence of HIV infection in pregnant women in Brazil is 0.4%[4]. Between 2000 and 2009, there was a total of 47,705 HIV-positive pregnant women, with 2,095 of these cases situated in the north of the country[3]. Reducing vertical HIV transmission becomes viable when seropositive pregnant women are identified and treated prophylactically with antiretroviral drugs during pregnancy and delivery, and the newborn infant also is treated at birth[5]. Important prerequisites for the implementation of these measures include access to and the factual use of health-care services during pregnancy and delivery and in the postpartum, which must include adequately trained health-care professionals, pre- and post-screening counseling, available and reliable free-of-charge HIV testing, and a well-equipped and adequate laboratory in which to monitor HIV-related blood parameters[6].

The Paediatric AIDS Clinical Trial Group protocol 076 (ACTG 076) has been recommended by the Brazilian Ministry of Health since 1996, and antiretroviral therapy has been made available in antenatal services and maternity clinics. Brazil adopts the policy of voluntary HIV counseling and testing for all pregnant women[3]. Notification of HIV-positive pregnant women cases and infants exposed to the risk of HIV transmission is compulsory (Decree no. 933 of September 4, 2000). In addition to the epidemiological aspects, the objective of implementing this measure concerns the important

operational nature of evaluating the interventions[7]. Cases of vertical transmission represent 95.1% of AIDS cases in individuals younger than 14 years in Brazil. Between 1996 and June 2009, 10,739 cases of AIDS were identified in children younger than 5 years in the country, representing 2% of all cases[3].

Of the various forms of HIV transmission, mother-to-child transmission is the form that has the greatest impact on control of the infection. The Ministry of Health has prioritized a program to control vertical HIV-1 transmission in an attempt to reduce transmission rates to the levels found in the United States and Europe. In fact, the vertical transmission of HIV could be considered to be the macroeconomic result of the equation between the frequency of risk factors and the investments made to avoid it[8].

To increase the access of pregnant women to diagnostic tests of HIV infection, different initiatives have to be implemented to progressively decentralize HIV testing and the availability of CD4 cell counts and viral load tests[9]. Data on the number of infected pregnant women in the country as a whole remain sparse, and monitoring of the stages of prophylaxis to reduce vertical HIV transmission is deficient. Studies published in Brazil report a prevalence rate of vertical HIV transmission that ranges from 2.5% to 8.6% **(Table 1)**[10-20].

TABLE 1 - Studies on mother-child HIV transmission conducted in Brazil and published in the literature.

Author	Year	Location (city, state)	Number	% (95% CI)
Tess et al.	1998	São Paulo, SP	434	16.0 (13.0-20.0)
Nogueira et al.	2001	Rio de Janeiro, RJ	145	2.8 (0.1-5.4)
João et al.	2003	Rio de Janeiro, RJ	297	3.6 (1.5-5.7)
Mussi-Pinhata et al.	2003	Ribeirão Preto, SP	239	8.6 (5.0-13.0)
Fernandes et al.	2005	Campos, RJ	44	6.8 (1.4-18.7)
Miranda et al.	2005	Vitória, ES	208	3.1 (0.8-5.5)
Kakehasi	2005	Belo Horizonte, MG	900	6.2 (4.8-8.1)
Dal Fabbro et al.	2005	Campo Grande, MS	76	2.5 (1.0 to 6.0)
Torres et al.	2007	Porto Alegre, RS	389	2.8 (1.2-4.4)
Succi Menezes	2007	Brazil	2,924	8.6 (7.2-10.2)* 7.1 (5.8-8.6)**
Tornatore et al.	2010	Rio Grande, RS	144	4.9 (1.4-8.4)

HIV: human immunodeficiency virus, **95% CI:** 95% confidence interval, **SP:** São Paulo, **RJ:** Rio de Janeiro, **ES:** Espírito Santo, **MG:** Minas Gerais, **MS:** Mato Grosso do Sul, **RS:** Rio Grande do Sul.

*Related to year 2000, **Year 2001.

The objective of the present study was to determine sociodemographic characteristics of HIV-infected pregnant women and the rate of mother-to-child transmission of HIV in Manaus, Amazonas, Brazil.

METHODS

This study was submitted to and approved by the internal review board of the Amazonas Tropical Medicine Foundation (FMTAM). Written consent was given by the patients for their information to be stored in the hospital database and used for research.

A cross-sectional descriptive study based on data from notification records and patient charts (complementing data) for the period ranging from 2007 to 2009 was conducted with HIV-positive pregnant women living in Manaus. The data were provided by the Amazonas State Coordination for Sexually Transmitted Diseases/AIDS.

To collect epidemiological data on vertical HIV transmission, an analysis was made of the data contained in the Notifiable Diseases Database of the State of Amazonas, and a search was made of the pregnant patient charts to complement some information.

The following data were extracted from the database of HIV-positive pregnant women: age, race, education level, time at which HIV was diagnosed, whether the patient had had prenatal care, type of delivery, prophylaxis with antiretrovirals during pregnancy and delivery, prophylaxis for the newborn infant, length of time and starting date of antiretroviral use by the newborn infant, and diagnosis of HIV infection in the child. Notification data that were incomplete were updated with information from the patient's medical charts or from the birth registries of the municipal maternity hospitals.

Statistical analysis was performed using a database in Excel spreadsheet format (Microsoft® Office, Excel 2003) and the Minitab software program, version 14. First, a descriptive analysis was performed that included the frequency distribution of qualitative variables and measures of central tendency for quantitative variables. The frequency of the diagnosis in question was estimated, together with the respective 95% confidence intervals.

Bivariate analysis was then performed to check for the presence of association between the variables. Chi-square (χ^2) tests were used for proportion differences, and Student's t tests and variance analysis were used for testing differences between mean values. To estimate associations with vertical HIV transmission, the odds ratio was used as a measure of association, estimated with a 95% confidence interval. Multivariate analysis was performed to estimate joint effects of independent variables, through the use of logistic regression models.

RESULTS

Notification of HIV infection was received for 509 pregnant women in Manaus between 2007 and 2009. In 2007, 152 cases were notified, with an incidence rate of 4.1 cases per 1,000 pregnant women. There were 186 notified cases (4.9 cases per 1,000 pregnant women) in 2008 and 171 cases (4.5 cases per 1,000 pregnant women) in 2009. The mean age of the women was 27 years (SD: ± 5.7 years; range: 13-45 years). The majority (478 women; 94%) lived in urban areas, whereas 21 (4%) lived in rural areas, and only three women resided in suburban areas.

The vertical transmission rate in this period was 9.9% (95% CI: 7.2-12.6%). Calculation of the vertical transmission rate was based on 48 cases of HIV-positive infants in the 487 pregnant women delivered, and in the remaining 22 cases, the pregnancy resulted in miscarriage.

The demographic data of the pregnant women in this study are described in **Table 2**. The majority of women were in the 20- to 29-year age group (60.6%; n = 308). Most of the women (54.8%) had not completed elementary school (eighth grade), whereas 128 had completed high school, and only 13 women had graduated from university. In 115 (22.6%) women, the diagnosis of HIV infection was made prior to pregnancy, whereas in 302 (59.3%), diagnosis was made during prenatal care, in 70 (13.8%) cases during delivery, and in 22 (4.3%) cases following delivery. Of the 509 women, 404 (79.4%) had attended prenatal care.

A total of 298 (58.6%) women initiated prophylactic HIV treatment during pregnancy. In 198 (38.9%) cases, delivery was

TABLE 2 - Characteristics of the HIV-positive pregnant women notified between 2007 and 2009.

Variables	Number	Percentage	95% CI*
Year of notification			
2007	152	29.9	25.9-33.8
2008	186	36.6	39.7-39.7
2009	171	33.5	38.5-38.5
Age group			
13-19 years	34	6.5	5.4-11.9
20-29 years	308	60.6	53.6-62.1
30-39 years	154	30.3	26.1-34.0
> 40 years	13	2.6	1.9-5.1
Education level			
illiterate	2	0.4	0.1-1.4
elementary school	279	54.8	40.4-55.9
high school	128	25.1	21.9-28.9
university	13	2.6	1.2-6.7
data missing	87	17.1	13.7-19.8
Prenatal care			
yes	404	79.4	76.3-83.4
no	83	16.3	12.8-19.3
miscarriage	22	4.3	2.6-6.4
Diagnosis of HIV			
prior to pregnancy	115	22.6	19.2-26.6
during prenatal care	302	59.3	54.9-63.7
during delivery	70	13.8	10.8-17.0
following delivery	22	4.3	2.8-6.6

HIV: human immunodeficiency virus, **%:** percentage, **95% CI:** 95% confidence interval of frequency in the population.

TABLE 3 - Vertical HIV transmission prophylaxis in pregnant women notified between 2007 and 2009.

Variables	Number	Percentage	95% CI*
Use of antiretroviral during pregnancy			
yes	298	58.6	49.1-68.2
no	135	26.5	19.7-31.1
data missing	54	10.6	4.0-12.2
not applicable*	22	4.3	2.5-6.1
type of delivery			
vaginal	198	38.9	23.6-48.0
elective cesarean	228	44.8	38.1-59.2
emergency cesarean	61	12.0	7.1-19.5
not applicable*	22	4.3	2.5-6.1
Use of antiretroviral during delivery			
yes	278	54.6	45.8-64.5
no	155	30.5	26.8-44.5
data missing	54	10.6	6.2-13.6
not applicable*	22	4.3	2.5-6.1
outcome of pregnancy			
live born infant	481	94.5	87.4-99.8
stillborn infant	6	1.2	0.5-3.4
miscarriage	22	4.3	2.5-6.1
Initiation of antiretroviral therapy in the newborn			
in the first 24h	317	62.3	52.7-72.4
more than 24h after delivery	32	6.3	3.5-7.9
not applicable*	22	4.3	2.5-6.1
not used	138	27.1	17.9-43.1
HIV-positive newborn infant			
yes	48	9.9	7.2-12.6
no	439	90.1	87.4-92.7

HIV: human immunodeficiency virus, **n:** number, **%:** percentage, **95% CI:** 95% confidence interval of frequency in the population.

*Not applicable: patients excluded due to miscarriage, **95% CI: 95% confidence interval of frequency in the population.

vaginal, whereas in 228 (44.8%), an elective Cesarean section was performed, and in 61 (12%) cases, the women were submitted to an emergency Cesarean section. Of the liveborn infants, 317 (62.3%) initiated treatment with antiretrovirals in the first 24 h after birth and 32 (6.3%) after the first 24 h, whereas 138 (27.1%) were not submitted to prophylactic antiretroviral treatment **(Table 3)**.

When the HIV-positive infants were compared with the HIV-negative ones in the bivariate analysis, residing in a rural area (8.3% versus 3.7; p = 0.002) was found to be a risk factor for vertical transmission, whereas having a diagnosis of HIV infection prior to or during pregnancy (41.7% versus 61.2%; p = 0.001), prophylactic antiretroviral therapy for the infant (31.3% versus 54.7%; p = 0.001) and delivery by elective Cesarean section (27.1% versus 46.9%; p = 0.010) constituted protective factors.

In the final multivariate logistic regression model, living in an urban area [OR = 0.7 (95% CI: 0.35-0.89)] and having had prenatal care [OR = 0.1 (95% CI: 0.04-0.24)] remained as protective factors against vertical HIV transmission in this population **(Table 4)**.

TABLE 4 - Multivariate analysis of factors associated with HIV vertical transmission among pregnant women notified in Manaus between 2007 and 2009.

Factors	Adjusted Odds ratio	95% CI	p value
Living in an urban area (yes versus no)	0.71	0.35-0.89	0.018
Attending prenatal care (yes versus no)	0.13	0.04-0.24	0.009
HIV diagnostic during pregnancy or delivery versus HIV diagnostic before pregnancy	1.48	0.79-2.73	0.215
HIV prophylaxis during pregnancy (yes versus no)	0.81	0.63-1.10	0.119
HIV prophylaxis during delivery (yes versus no)	0.75	0.36-1.54	0.434
HIV prophylaxis in the first 6h after delivery (yes versus no)	0.50	0.11-2.24	0.366
Delivery (vaginal versus cesarean section)	1.22	0.76-1.97	0.415
Pregnancy outcome (stillborn/miscarriage versus alive)	1.48	0.87-2.51	0.149

HIV: human immunodeficiency virus, **95% CI:** 95% confidence interval.

DISCUSSION

The rate of vertical HIV transmission in Manaus between 2007 and 2009 was 9.4%. In a multicenter study conducted in Brazil, Menezes Succi reported a rate of vertical transmission of 7.1% (95% CI: 5.8%-8.6%) in 2001 for Brazil as a whole, ranging from 4.9% in the midwest to 17.6% in the north[19]. The prevalence in the present study, although still high, was lower than the value calculated for the northern region in the multicenter study.[19] This may be explained by the fact that Manaus is not representative of the entire region because it is the largest city in terms of urban area and probably has better health-care facilities compared with the other municipalities in the region. Furthermore, the health conditions in the region improved after the previously conducted 2001 study.

The rate of vertical transmission in Manaus identified in the present study is in agreement with that found in other studies carried out in Brazil, which range from 2.5% to 8.6%[10-20]. These rates found in Brazil are higher than those reported in studies published in Europe, where prophylactic measures are implemented early in pregnancy, resulting in mother-to-child transmission rates of around 1%[21-25].

The mean age of the HIV-positive pregnant women in the present study was 27 years. In Brazil, 55% of notified cases of pregnant women with AIDS fall within the 20- to 29-year age group[3]. The majority of seropositive pregnant women in Manaus (54.8%) had, at most, some elementary education. Approximately 50% of the HIV-positive women in Brazil have between 1 and 7 years of schooling[3]. The poor education level of these women hampers their access to information on HIV, placing the woman and her family at an even greater risk of HIV transmission[18].

Delayed diagnosis of HIV infection may have been the reason in the present study for the fact that less than 70% of the seropositive women used antiretrovirals during pregnancy to prevent vertical transmission. The fact that 79.4% of the patients stated that they had undergone prenatal care is relevant. The Sentinel Childbirth Study conducted in 2004 reported that only 62.5% of the women giving birth had undergone HIV testing during pregnancy and were aware of the result of their test prior to being admitted to hospital for delivery[4]. Other studies conducted in Brazil also have reported the difficulty of access to prenatal care and problems in blood sampling and in receiving the results of HIV screening tests during pregnancy and delivery[14, 26, 27]. These data show that prophylactic actions related to vertical HIV transmission remain deficient with respect to prevention and care. This situation is aggravated when it is taken into consideration that the act of providing a blood sample for testing does not guarantee that the woman will receive the results of her test, which would permit awareness of her HIV serological status and consequently enable preventive measures to be implemented.

The situation also differs from country to country. In 2008, 45% of HIV-positive pregnant women in Sub-Saharan Africa were receiving antiretrovirals[1]. In Botswana, 37% had begun highly active antiretroviral therapy during pregnancy, whereas 42% were using only zidovudine prophylactically, and 21% received no medication at all during pregnancy[28]. In Asia, only 25% of pregnant women had access to antiretrovirals[1]. In Western Europe and in the United States, vertical transmission is considered to be under control[29].

In the present study, 54.6% of the women received zidovudine in the maternity hospital, whereas 30.5% were not treated prophylactically at the time of delivery in Manaus, and the remaining women miscarried prior to initiating prophylaxis. In a study carried out in the Brazilian State of Maranhão, 78.5% of seropositive pregnant women failed to receive adequate prophylaxis to prevent vertical transmission, and 55% of the babies were delivered vaginally[30]. This high rate of vaginal delivery, which also was found in the present study, has been reported by other authors.[31, 32] Of the deliveries carried out in HIV-positive pregnant women in Manaus during the study period, 38.9% were vaginal, whereas 56.8% of the women were submitted to Cesarean section. Nevertheless, Cesarean sections were elective in only 44.8% of these patients, whereas in the remaining 12%, they occurred as the result of an obstetric emergency in which labor had already begun and amniotic membrane rupture may already have occurred, a situation that may incur a risk of transmission at the moment of delivery.

In Manaus, 62.3% of the infants were treated with antiretrovirals within 24 h of birth, whereas almost 30% were not submitted to prophylaxis. The data found in the present study are disquieting and reveal a severe shortcoming in maternal and child health care, particularly with respect to the prevention of vertical HIV transmission during pregnancy. In other states in Brazil, antiretroviral use was much higher[15, 18]. The low use of antiretrovirals as prophylaxis during pregnancy in Manaus is probably the result of the delayed diagnosis of HIV infection in pregnant women. These findings raise other questions such as the following: Was there a delay in initiating prenatal care? When the tests were performed, were the results provided in time? Was prenatal care being provided by a multidisciplinary team in a complete and satisfactory manner as appropriate for the care of an HIV-positive pregnant woman?

The present study is unable to provide answers to these questions in view of the limited data available in the databases, patient charts, and registries of the maternity hospitals; however, it is important to highlight the role of prenatal care in adopting strategies for reducing vertical HIV transmission.

Although antiretroviral therapy is offered universally in Brazil, the proportion of HIV-positive pregnant women who do not have access to the prophylactic measures recommended by the National Department of Sexually Transmitted Diseases/AIDS and Viral Hepatitis, and who ultimately fail to be tested for HIV, remains high, either as a function of the women's social condition or due to inadequacies in the health-care system. Late detection of HIV infection during prenatal care represents an opportunity to intervene in the case of the HIV-infected patient that is lost, thus limiting the possibilities of reducing the number of pediatric cases caused by vertical transmission[4].

Adequate prenatal care implemented early in pregnancy and access to HIV testing are measures that are crucial to achieving a reduction in vertical transmission rates. Based on the findings of the present study, the relevance of adequately complying with measures that have proven effective in reducing HIV transmission in the maternal and pediatric populations should be emphasized. These actions should be carried out by a trained multidisciplinary team. The social and economical impact of these measures on the country is potentially significant.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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